METHODS OF ASSESSING A TISSUE INFLAMMATORY RESPONSE USING EXPRESSION PROFILES OF ENDOTHELIAL CELLS

Field of the Invention

The present invention relates to gene expression profiles of endothelial cells and to the use of these profiles in the assessment of disease conditions and in therapy.

Background to the Invention

The migration of leucocytes into tissues is a key part of the normal function of the immune system, mucosal surfaces, the uterine endometrium, mammary gland and ovary. However, emigration of leucocytes from the intravascular space into the tissues can also be stimulated by the inflammation response. Inflammation is a response of the body to damage or infection, and typically involves movement of leucocytes and proteins across endothelial walls and into tissues.

The inflammation response involves a number of signalling molecules. Some of these act on the endothelium to cause the endothelial cells to adhere less tightly to one another and/or to make their surfaces adhesive to passing white blood cells. Other signals act as chemoattractants for the leucocytes, or promote expression of adhesion molecules on the leucocytes. Yet other signals regulate leucocyte activation and survival.

Signalling molecules include 'quick release' mediators that are involved in increased vascular permeability, such as histamine. These act synergistically with the later stage 'process induced' mediators. These later stage mediators include chemokines, which attract leukocytes into areas of inflammation, and cytokines, subsequently released from inflammatory cells and activated endothelial cells.

TNF-α, IL-1β and IL-8 are inflammatory mediators found at high concentrations at sites of inflammation, and endothelial cells possess receptors for these mediators (1-3).

TNF-α is a prototypical cytokine, which was originally isolated from macrophages, but is now known to be generated by a variety of cells, including lymphocytes, monocytes, neutrophils, T-cells, myocytes and smooth muscle cells. TNF receptor 1 engagement by TNF-α leads to the initiation of apoptosis in a wide variety of cell types. Receptor binding also results in sustained NF-κB activation, required for expression of a repertoire of genes involved not only in the inflammatory response, but also increased cell survival and enhanced resistance to TNF-α-induced apoptosis. Signalling pathways also activated in endothelial cells by TNF-α include the phosphatidylinositol (PI) kinase dependent kinases, stress activated protein kinases (SAPK) and mitogen activated protein kinases (MAPK) (3, 4).

IL-1β is another prototypical cytokine. The main source of secreted Il-1β is monocytes, but it is also generated by a wide variety of other cell types, including, notably, activated macrophages, neutrophils, platelets, T- and B-cells, natural killer (NK) cells, endothelial cells, SMCs (smooth muscle cells) and fibroblasts. IL-1β is synthesised as a precursor and, once proteolytically cleaved, can activate many cell types with roles in immunity and inflammation. As with TNF-α, IL-1β activates the NF-κB (nuclear factor κB) survival pathway, as well as MAPK cascades p42/p44, p38 and Jnk (5).

IL-8 is a chemokine that has been closely linked with angiogenesis. The main sources of IL-8 are monocytes, neutrophils, T-cells, NK cells, endothelial cells, fibroblasts and epithelial cells. IL-8 is involved in the process of

leukocyte transmigration into tissues, as well as other aspects of the inflammatory response. Its production is not constitutive but is induced by pro-inflammatory cytokines. IL-8 binds to heparin and induces endothelial cell migration, proliferation and survival in vitro (6). IL-8 and its receptors appear to be critical in angiogenesis and tumour progression (7, 8).

Molecular mediators of inflammation such as TNF-α, IL-1 and IL-8 act on target cells within inflamed tissues such as endothelial cells, fibroblasts and leukocytes. The effects of combinations of inflammatory mediators such as these three is synergistic - i.e. the action of these factors 'in concert' is likely to be different from the sum of their individual effects.

The inflammatory response of tissues, such as is typified in inflammatory diseases, typically involves the abnormal or excessive movement of leucocytes and proteins into the tissue. This can result in a large number of acute or chronic inflammation disorders. Leucocyte and protein movement can also play a role in conditions which are not primarily inflammatory diseases, but in which the tissues demonstrate an inflammatory response. For example, the diseases of atherosclerosis and endometriosis may rely on the migration of leucocytes into the lesions. Repair of tissue necrosis that occurs in stroke or heart attack also requires inflammation responses. Tumour growth may be regulated by leucocytes that migrate from the blood into the tumour. These leucocytes release factors that directly promote tumour cell growth and tumour angiogenesis. In addition, leucocytes that migrate into tumours mediate an immune responses towards tumour cell-specific antigens with subsequent anti-tumour effect. The role of inflammation in tumour growth is therefore complex,

and involves a balance between stimulatory and inhibitory pathways.

In view of the role of inflammation responses in a wide variety of pathological conditions, there is a continuing need for the development of methods for the assessment or treatment of human medical conditions associated with such responses. In addition, inflammation responses are essential features of physiological processes such as female fertility and wound healing. There is a need for methods to modulate inflammatory responses in order to modulate these processes.

Disclosure of the Invention

We have analysed the changes in transcript abundance which occur when human umbilical vein endothelial cells (HUVECs) are contacted with a mixture of TNF-α, Interleukin-1β and Interleukin-8. These factors are typically present at increased concentrations in tissues during an inflammatory response and are secreted by a wide variety of cell types over sustained periods.

Primary cell cultures of endothelial cells derived from a number of different individuals were tested in order to obtain a consensus set of transcripts regulated in endothelial cells of multiple individuals during an inflammatory response. Data were analysed using a novel combination of bio-informatic algorithms, including a modified Loess normalisation and a CyberT algorithm.

In addition, we analysed expression in different endothelial cells types obtained from different parts of the body, namely HUVEC, human coronary artery endothelial cells (HCAEC) and human uterine microvascular endothelial cells (UtMVEC). It was found that many transcripts, including those which were

most strongly regulated in HUVECs, were consistently regulated by inflammatory signals in all three cell types.

Thus, in the present invention we have used a novel methodology to identify for the first time a pattern of changes in the regulation of expression of certain genes in endothelial cells responding to inflammatory signals as well as a consensus set of genes whose transcripts are modified in response to inflammatory signals in endothelial cells derived from many individuals, and which are therefore likely to have wide applicability to populations of patients.

Accordingly, the present invention provides a means for assessment of (e.g., diagnosis, prognosis or monitoring of) a tissue inflammatory response or a condition associated therewith. Such a response is typically associated with one of a number of conditions and it may also involve the migration of leucocytes across an endothelium. Therefore, by determining a tissue inflammatory response, a determination may also be made of the condition with which that response may be associated. Also, the finding that a number of transcripts are regulated in these responses and hence conditions, both of genes known as such and from ESTs, allows the provision of novel assay targets and the development of new therapies for such conditions.

Accordingly, in a first aspect, the present invention provides a method of assessing a tissue inflammatory response, comprising:

making a quantitative determination of the level of at least five transcripts shown in Table 1, or proteins encoded thereby, in a sample; and

comparing the abundance of said transcripts or proteins so determined with the level of said transcripts or proteins obtained from a control sample of cells.

Preferably, the sample comprises cells obtained from a site within a patient believed to be affected by a tissue inflammatory response, suitably endothelial cells, or patient blood, serum or urine.

In another aspect, the invention provides a gene chip array suitable for use in the above-described method of the invention, comprising at least five nucleic acids suitable for detection of at least five transcripts shown in Table 1; optionally a control specific for said transcripts; and optionally at least one control for the gene chip.

In a further aspect, the invention provides a protein based assay suitable for use in the above-described method of the invention, for the assessment of at least five proteins encoded by transcripts including those shown in Table 1; optionally a control specific for said proteins; and optionally at least one control for the assay.

In a further aspect, the invention provides an assay method for determining a modulator of a tissue inflammatory response or a condition associated therewith, wherein said method comprises

a) providing a protein encoded by transcripts from Table 1;
b) bringing the protein into contact with a candidate modulator of its activity;
c) determining whether said candidate modulator is capable of modulating the activity of the protein;

or wherein said method comprises;

a) providing an endothelial cell in culture;
b) bringing said cell into contact with a candidate modulator of said tissue inflammatory response; and
c) determining whether said candidate modulator is capable of modulating the level of at least one transcript selected from the transcripts of Table 1.

Modulators obtained by such methods may be used in a method of modulating tissue inflammatory responses in a human or animal subject, e.g., so as to treat a condition discussed below.

In another aspect, the identification of genes of previously unknown function and of ESTs, has allowed new potential targets for therapeutic intervention to be developed. Thus, the invention provides a vector comprising a sequence encoding a transcript from Table 1b operably linked to a promoter for the transcription of said sequence. Such vectors are useful in the expression of proteins which may be therapeutics or therapeutic targets. The vectors may also have direct therapeutic use in themselves, e.g., in gene therapy applications.

Description of the Tables

Table 1a lists transcripts of genes whose levels are regulated in endothelial cells by inflammatory mediators TNFα, IL-1β, and IL-8, where the genes have a previously ascribed function.

Table 1b lists transcripts of genes or ESTs whose levels are regulated in endothelial cells by inflammatory mediators TNFα, IL-1β and IL-8, where the genes/ESTs do not have a previously ascribed function.

Table 2a provides nucleic acid sequences for each of the probes mentioned in Table 1a.

Table 2b provides nucleic acid sequences for each of the probes mentioned in Table 1b.

Detailed Description of the Invention

Reference herein to Table 1 and 2 is to be construed as meaning Tables 1a or 1b together, or Tables 2a and 2b together, respectively, unless the context is explicit to only one of these component parts of Table 1 or Table 2 respectively.

Conditions associated with tissue inflammatory responses

In its first aspect, the present invention is concerned with a method for the assessment of a tissue inflammatory response. It is generally recognised, as is discussed above, that leucocytes are involved in the inflammatory responses of tissues. An inflammatory response may involve the movement of leucocytes across an endothelium. However, proteins which are involved in such an inflammatory response may also cause the movement of leucocytes to the inflamed tissue, may participate in or be responsible for the activation of the leucocytes, the activation and angiogenesis of endothelial cells, or may influence the inflammatory response by inhibiting the apoptosis of leucocytes or endothelial cells.

A tissue inflammatory response is typically involved with a condition or disease state of the patient. By "condition" as used herein is meant any disease state or body response which involves, causes or is associated with the tissue inflammatory response.

The tissue inflammatory response may either be excessive or unwanted, for example as may be the case in an inflammatory disease such as those discussed herein below, or may be insufficient, such as, for example in conditions associated with defective adhesion proteins, such as leucocyte adhesion deficiency types 1 and 2 (LAD-1 and LAD-2).

Tissue inflammatory responses and trans-endothelial leucocyte movement can be affected by changes in the endothelial cells, for example by changes in adhesion molecule expression, which alters the ability of the leucocytes to adhere to the endothelial cells, or alters the chemokine-mediated recruitment of leucocytes to the inflammed tissue. In respect of the present invention, it is preferred that the changes in the endothelial cells are in response to an inflammatory signal.

A condition to be assessed by the method of the invention may be one in which endothelial cells in the location of the inflammatory response or affected by the inflammatory response are altered so as to promote an inflammatory process and allow the movement of leucocytes across that endothelium.

Typically the movement of leucocytes across an endothelium occurs as a response to inflammatory signals. Therefore, a tissue inflammatory response to be assessed by the method of the invention is one in which inflammatory signals are issued. Exemplary of such conditions are inflammatory diseases, vasculitic syndromes, atherosclerosis and associated diseases, conditions involving tumour growth and chronic transplant rejection.

Inflammatory diseases include inflammatory bowel disorders, psoriasis, ischemic reperfusion, adult respiratory distress

syndrome, asthma, allergic rhinitis, dermatitis, meningitis, encephalitis, uveitis, diseases involving leucocyte diapedesis, central nervous system inflammatory disorders, Alzheimer's, endometriosis, multiple sclerosis, multiple organ injury syndrome, alcoholic hepatitis, bacterial pneumonia, antigen-antibody complex mediated diseases; inflammation of the lung (including pleurisy, alveolitis, pneumonia, chronic bronchitis, bronchiectasis, cystic fibrosis and COPD), vasculitis, polyarteritis nodosa, giant cell arteritis, microscopic polyarteritis, pre-eclampsia and autoimmune diseases (such as rheumatoid arthritis, Sjorgen's syndrome, and the multiple forms of renal failure which are primarily due to autoimmune attack directed at the endothelial cells in the kidney glomeruli).

In atherosclerosis and associated diseases, such as coronary heart disease, peripheral vascular disease and cerebrovascular accident, leucocyte migration across the endothelial layer into blood vessel walls at the site of an atherosclerotic plaque is driven by inflammatory signals from leucocytes associated with the plaque and the underlying endothelial cells. Plaque instability and subsequent rupture leading to thrombosis and vessel stenosis or occlusion may be associated with inflammatory effects on the endothelial cells within the area of the plaque.

Tumour growth may be regulated by leucocytes that migrate from the blood into the tumour, and which release factors that directly promote tumour cell growth and tumour angiogenesis. Thus, cancers and especially those involving solid tumours may also be a relevant therapeutic indication.

Chronic transplant rejection critically involves immune cell migration across blood vessels and immune attack directed

towards endothelial cells and hence is suitable for assessment by the method of the invention.

These and other conditions associated with the release of inflammatory signals may be the subject of methods of the present invention.

Assessment of a tissue inflammatory response

In the present invention, it will be understood that the determination of cells "obtained from a site" believed to be affected by a tissue inflammatory response is reference to an *in vitro* method practiced on a sample after removal from the body. The step of removing the sample, e.g., by biopsy, is not part of the invention as such.

In addition to or as an alternative to techniques such as tissue biopsies, bodily fluids such as blood, serum and urine may be collected to reveal inflammation-induced changes within these fluids. Such changes may be demonstrated by, for example, an alteration in the sample in the abundance of endothelial cell-derived proteins that are encoded by the sequences in table 1.

Accordingly, the present invention provides a method for the diagnosis of a condition with which a tissue inflammatory response is associated comprising the determination of the abundance of endothelial cell-derived proteins encoded by at least five of the transcripts of Table 1 in a sample from a patient suspected of suffering from such a condition.

As explained above, the data obtained in the present invention shows that contacting endothelial cells with TNFα, IL-1β and IL-8 results in characteristic changes to certain transcripts, taking into account variation between individuals and between

different endothelial tissues. These changes may take the form either of a pattern of response or may affect individual transcripts. Accordingly, it is possible to use these characteristic changes as a reference for the diagnosis of conditions such as those discussed above.

In addition to, or as an alternative to, diagnosis, assessment of the condition may be a determination of the severity or precise clinical sub-type of the condition. It may also be a method of prognosis of the future course of the condition. Furthermore assessment can be over a period of time, for example in the monitoring of the treatment of a condition.

In its first aspect, the present invention provides a method of assessing a tissue inflammatory response by comparing the transcript levels in a sample taken from a patient showing an inflammatory response with the transcript levels of the same genes in a control sample.

As discussed above, the sample may be either of cells from a specific tissue demonstrating an inflammatory response, such as endothelial cells, or may alternatively be of a protein-containing bodily fluid, such as blood, serum or urine.

A control sample for the above methods is typically a sample of unaffected cells, that is cells from a tissue not demonstrating a tissue inflammatory response or cells believed not to be affected by the condition. It is preferred that the test and control sample are both of the same cell type and more preferred that the test and control sample are of endothelial cells. Most preferably, the test and control sample are of the same endothelial cell type, i.e. from the same tissue location.

If required, the control sample may be taken from a population of subjects. Where a population of subjects is used, the comparison may be made with the average (e.g., mean or median) transcript level in samples of cells from said population. Affected tissue may also be used as a control. Typically the affected tissue will be from a patient other than that from which the test sample was taken. It is generally preferred that, if affected tissue is being used as a control, the patient from which that sample is removed has or is believed to have the same condition as the patient from which the test sample is removed.

In some embodiments, the method of the invention may comprise the use of more than one control; for example the sample to be tested may be compared to a normal or unaffected sample from the same patient and the transcript level of an affected sample from another patient or patients.

As discussed above, the method of the invention allows for the monitoring of a condition, either before, during or after treatment. Where the test sample is from a patient having or believed to have tissue inflammation, it is generally preferred that a sample is also obtained from the patient at an earlier time point, so as to provide a historical record.

In another embodiment, the method allows for assessment of the effectiveness of a particular treatment. By comparing the severity of the tissue inflammation in a single patient at two or more time points, it is possible to determine whether or not a particular treatment regime is having a positive effect. The effectiveness of any one regime may differ from patient to patient, or during the course of the disease.

In a preferred embodiment, the invention is performed by looking at the level of a plurality of gene transcripts or plurality of proteins derived from these transcripts. This is because we have found that between individual subjects, the transcript level of individual genes may vary. It is therefore desirable that the transcript level is assessed for several genes. For example, it may be assessed for at least 5, preferably at least 10 and more preferably at least 20 transcripts or proteins derived from transcripts of Table 1.

The level of expression may be determined either for the genes or proteins individually or in specific combinations, or a pattern of expression of a plurality of genes may be determined.

In the first aspect of the present invention, the level of the transcripts assessed is compared in a test and a control sample. It may be that the response to an inflammatory signal causes the level of the transcripts either to rise or to fall. Hence there may be either up-regulation of the transcripts in response to an inflammatory signal or down-regulation. It is not important to the present invention whether there is either up-regulation or down-regulation, but rather that there is change from the control.

As an aid to determining the difference in transcript or protein regulation between a test and a control sample, the specific amount of up- or down-regulation may be determined. This can be expressed as a "fold" increase or decrease. It is not important to the present invention how large is the increase or decrease in transcript level, but rather it is important that there is a significant change from the control. In the present invention it is generally preferred that there be at least a two-fold change, i.e. increase or decrease, in

the transcript level. There is no upper limit on the amount of increase or decrease in transcript or protein level, but we have found that a 50-fold change in the level of certain transcripts and apparent *de novo* upregulation of certain proteins can be demonstrated.

Furthermore, in the assessment of up- or down-regulation of transcript or protein levels, it is not necessary for all transcripts or proteins being assessed to be regulated by the same amount. Of more significance in this respect is the establishment of a pattern of regulation.

In one embodiment of the present invention, the transcripts or proteins assessed may include one or from transcripts from one or more families or groups of protein. Preferably, the method involves determining the levels of at least one transcript or protein in two or more of such families or groups of protein, preferably three, four, five or more, and more preferably each of such families or groups of protein.

Typical such groups or families include proteases, bone morphogenetic proteins, cell signalling proteins, proteins involved in transcriptional regulation, enzymes, cell cycle regulation proteins, cell communication proteins, nuclear proteins, complement proteins, extracellular matrix proteins, proteosomes, heavy metal binding proteins, TNF-receptor superfamily proteins, HLA proteins, cell adhesion proteins, cytokines/chemokines, cytokine/chemokine receptors, cytoskeletal proteins, regulators of apoptosis, growth factors and growth factor receptors.

It is generally preferred that the transcripts or proteins assessed include one or more selected from cytokines/-chemokines, cytokine/chemokine receptors, cytoskeletal

proteins, extracellular matrix protins, regulators of apoptosis, growth factors and growth factor receptors.

Of particular interest to the method of the present invention is the regulation of particular transcripts or proteins. These can be assessed either per se or as part of a pattern of regulation. Therefore, in the method of the present invention, it is preferred that the transcripts or proteins assessed include one or more of: colony stimulating factor 3 (granulocyte), colony stimulating factor 2 (granulocyte-macrophage), granulocyte chemotactic protein 2, diubiquitin, ELAM-1, TNF-induced protein 6, Exodus 1, IL-1β, VCAM-1, ICAM-1, IAP1, TNF-inducible A20, RIPK2, MMP 10, TRAF1, JAK binding protein, dual specificity phosphatase 4, IL-6, IL-8, Gro-gamma, MCP-1, Gro-beta, Gro-alpha, ENA-78, fractalkine, small inducible cytokine subfamily A14, small inducible cytokine A5, LI7 receptor, toll/interleukin 1 receptor-like 4, CCAAT, MAD-3, COX-2, Mn SOD, NO synthase, L-kynurenine hydrolase, tissue factor pathway inhibitor 2, laminin gamma 2, Toll-like receptor 2, natural killer cell transcript 4, TNF-alpha induced protein 2, cationic amino acid transporter 2A, fatty acid binding protein 4, TNF receptor superfamily member 11b and TNF superfamily member 9.

It is more preferred that in the method of the present invention the transcripts or proteins assessed include one or more of: colony stimulating factor 3 (granulocyte), colony stimulating factor 2 (granulocyte-macrophage), granulocyte chemotactic protein 2, diubiquitin, ELAM-1, TNF-induced protein 6, Exodus 1 and IL-1β.

Alternatively, the method involves determining a pattern of expression of transcripts, wherein the transcripts include at least some of the transcripts illustrated in Table 1 herein.

The transcript or protein level of a gene or genes may be determined by any suitable means. Where many different gene transcripts are being examined, a convenient method is by hybridisation of the sample (either directly or after generation of cDNA or cRNA) to a gene chip array.

Where gene chip technology is used, the genes (this term used herein includes the ESTs of Table 1) are all present in commercially available chips from Affymetrix, and these chips may be used in accordance with protocols from the manufacturer. Generally, methods for the provision of microarrays and their use may also be found in, for example, WO84/01031, WO88/1058, WO89/01157, WO93/8472, WO95/18376/ WO95/18377, WO95/24649 and EP-A-0373203 and reference may also be made to this and other literature in the art.

Where many different proteins are being examined, a convenient method is antibody chip, multi-target ELISA, or proteomic analysis. Generally, methods for the provision of protein assays and their use may also be found in, for example, U.S. Patent 6,329,209 and U.S. Patent No. 2,656,508. Such methods are common within the art. Further information on such methods may be obtained by reference to http://www.marketresearch.com/map/prod/904611.html

Table 1 provides the names of genes and these may be used to obtain their DNA sequences and encoded protein sequences from databases such as Genbank. In addition, the particular sequences used on the Affymetrix chip we have used may be determined by the Affymetrix reference numbers supplied in the Table, which are publicly available and may be related directly to Genbank reference numbers. EST gene sequences in some cases are also given by Genbank reference numbers. Those

of skill in the art may refer to either of the Affymetrix reference number or the Genbank reference number in practicing the present invention.

Table 2 provides cDNA sequence information for each of the probes used on the Affymetrix chip that are also listed in Table 1. Table 1 lists the probe set used to obtain the specific protein/EST listed therein and Table 2 provides the cDNA sequence for each probe set mentioned in Table 1.

In Tables 2a and 2b, "n" represents in each case a region of the nucleic acid that was not probed by the probe set sequences on the gene chips. Thus, in order to make the arrays as specific as possible, only selected regions of the full cDNA's have been used, with the exclusion of some intervening sequences. Excluded sequences are those in which the single nucleotide code (a, g, c or t) has been replaced with "n".

Alternatively, or in addition, quantitative PCR methods may be used, e.g. based upon the ABI TaqMan™ technology, which is widely used in the art. It is described in a number of prior art publications, for example reference may be made to WO00/05409. PCR methods require a primer pair which target opposite strands of the target gene at a suitable distance apart (typically 50 to 300 bases). Suitable target sequences for the primers may be determined by reference to Genbank sequences as mentioned above.

Gene Chips

Although the prior art provides a gene chip which includes, as part of a very large array, the genes of one or more of Tables 1a and 1b, the identification of a relatively small set of genes of use in assessing the conditions discussed above

allows the provision of a small chip specifically designed to be suitable for use in the present invention (a tailored gene array).

Thus the invention provides a gene chip array comprising at least five nucleic acids suitable for detection of at least five transcripts shown in Table 1 (either directly or after generation of cDNA or cRNA); optionally a control specific for said transcripts; and optionally at least one control for said gene chip.

In an alternative embodiment of this aspect, the invention provides a gene chip array for detection of at least five transcripts shown in Table 1 comprising at least five nucleic acids selected from Table 2 capable of detecting the presence of said at least five transcripts; optionally a control specific for said transcripts and optionally at least one control for said gene chip.

The gene chip array comprises at least five different nucleic acids, preferably at least 10 or 20 different nucleic acids.

Desirably, the number of sequences in the array will be such that where the number of nucleic acids suitable for detection of the Table 1 transcripts (or the number of Table 2 sequences) is n, the number of control nucleic acids specific for individual transcripts is n', where n' is from 0 to 2n, and the number of control nucleic acids (e.g. negative controls or controls for detection of "housekeeping" transcripts, abundant endothelial cell transcripts, transcripts which have a higher level of expression in endothelial cells, transcripts which have a higher level of expression in the particular endothelial type being assessed, or the like) on said gene chip is m where m is from 0 to 100,

preferably from 1 to 30, then n + n' + m represent at least 50%, preferably 75% and more preferably at least 90% of the nucleic acids on said chip.

Protein Chips

As discussed above in relation to gene chips, the provision of the transcripts and proteins encoded thereby in Table 1 allows for the production of appropriate tailored protein chips. Such chips may be used in the form of an antibody chip, or may encompass multi-target ELISA, or proteomic analysis. Generally, methods for the provision of protein assays and their use may be found in, for example, U.S. Patent 6,329,209 and U.S. Patent No. 2,656,508. Such methods are common within the art.

Accordingly, in a further aspect, the present invention provides a protein based-assay suitable for use in the above-described method of the invention, for the assessment of at least five proteins encoded by transcripts including those shown in Table 1; optionally a control specific for said proteins; and optionally at least one control for the assay.

In a preferred embodiment, the protein-based assay is an antibody chip or ELISA, preferably multi-target ELISA.

Assay Methods

Assay methods of the present invention may be practiced in a wide variety of formats, for example on protein or nucleic acid components or in whole cells in culture.

The present invention provides in its second aspect an assay method for a modulator of a tissue inflammatory response or a condition associated therewith, comprising:

(a) providing a protein encoded by a transcript of Table 1;

(b) bringing said protein into contact with a candidate modulator of its activity; and

(c) determining whether said candidate modulator is capable of modulating the activity of said protein.

Where the response of an endothelial cell to inflammatory signals involves down-regulation of a transcript, the assay is preferably for an activator of the protein, and the assay preferably involves determining whether the modulator is capable of increasing the activity of the protein. In this embodiment, the assay may be carried out under conditions where the protein normally shows low or no activity.

Where the response of an endothelial cell to inflammatory signals involves up-regulation of a transcript, the assay is preferably for an inhibitor of the activity of the protein, and the assay preferably involves determining whether the modulator is capable of reducing the activity of the protein. In this embodiment, the assay may be carried out under conditions in which the protein is normally active.

In this assay method, the determination of modulation of activity will depend upon the nature of the protein being assayed. For example, proteins with enzymatic function may be assayed in the presence of a substrate for the enzyme, such that the presence of a modulator capable of modulating the activity results in a faster or slower turnover of substrate. The substrate may be the natural substrate for the enzyme or a synthetic analogue. In either case, the substrate may be labelled with a detectable label to monitor its conversion into a final product.

For proteins with a ligand binding function, such as receptors, the candidate modulator may be examined for ligand binding function in a manner that leads to antagonism or agonism of the ligand binding property.

For proteins with DNA binding activity, such as transcription regulators, the DNA binding or transcriptional activating activity may be determined, wherein a modulator is able to either enhance or reduce such activity. For example, DNA binding may be determined in a mobility shift assay. Alternatively, the DNA region to which the protein binds may be operably linked to a reporter gene (and additionally, if needed, a promoter region and/or transcription initiation region between said DNA region and reporter gene), such that transcription of the gene is determined and the modulation of this transcription, when it occurs, can be seen. Suitable reporter genes include, for example, chloramphenicol acetyl transferase or more preferably, fluorescent reporter genes such as green fluorescent protein.

Alternatively, or in a third aspect, the present invention provides an assay method for a modulator of a tissue inflammatory response or a condition associated therewith comprising:

(a) providing an endothelial cell in culture;

(b) bringing said cell into contact with a candidate modulator of said condition; and

(c) determining whether said candidate modulator is capable of modulating the level of at least one transcript selected from the transcripts of Table 1.

In the first step of this method, an endothelial cell is cultured. Any appropriate method may be used for the

harvesting and culture of the cells. Techniques for the culture of endothelial cells are common in the art.

Candidate modulator compounds may be natural or synthetic chemical compounds used in drug screening programmes. Extracts of plants, microbes or other organisms, which contain several characterised or uncharacterised components, may also be used. Combinatorial library technology (including solid phase synthesis and parallel synthesis methodologies) provides an efficient way of testing a potentially vast number of different substances for the ability to modulate an interaction. Such libraries and their use are known in the art for all manner of natural products, small molecules and peptides, among others. Many such libraries are commercially available and sold for drug screening programmes of the type now envisaged by the present invention.

A further class of candidate modulator comprises antibodies or binding fragments thereof which bind a protein target.

Examples of antibody fragments, capable of binding an antigen or other binding partner, are the Fab fragment consisting of the VL, VH, Cl and CH1 domains; the Fd fragment consisting of the VH and CH1 domains; the Fv fragment consisting of the VL and VH domains of a single arm of an antibody; the dAb fragment which consists of a VH domain; isolated CDR regions and F(ab')2 fragments, a bivalent fragment including two Fab fragments linked by a disulphide bridge at the hinge region. Single chain Fv fragments are also included. An antibody specific for a protein may be obtained from a recombinantly produced library of expressed immunoglobulin variable domains, e.g. using lambda bacteriophage or filamentous bacteriophage which display functional immunoglobulin binding domains on their surfaces; for instance see WO92/01047. Such a technique

allows the rapid production of antibodies against an antigen, and these antibodies may then be screening in accordance with the invention.

Another class of candidate molecules is peptides, based upon a fragment of the protein sequence to be inhibited. In particular, fragments of the protein corresponding to portions of the protein which interact with other proteins or with DNA, may be a target for small peptides which act as competitive inhibitors of protein function. Such peptides may be for example from 5 to 20 amino acids in length.

The peptides may also provide the basis for design of mimetics. Such mimetics will be based upon analysis of the peptide to determine the amino acid residues or portions of their side chains essential and important for biological activity to define a pharmacophore followed by modelling of the pharmacophore to design mimetics which retain the essential residues or portions thereof in an appropriate three-dimensional relationship. Various computer-aided techniques exist in the art in order to facilitate the design of such mimetics.

Cell based assay methods can be configured to determine expression of the gene either at the level of transcription or at the level of translation. Where transcripts are to be measured, then this may be determined using the methods of the first aspect of the invention described above, e.g. on gene chips, by multiplex PCR, or the like.

As above, where the transcript is one which is down-regulated in response to inflammatory signals, the assay is preferably for agents which increase the expression of the gene (e.g., by increasing the quantity of the transcript). Such an agent may

comprise the coding sequence of the gene itself (i.e., it may be a gene therapy vector). Where the transcript is one which is up-regulated in response to inflammatory signals, the assay is preferably for agents which decrease the expression of the gene.

Cell based assay methods may be used to screen candidate modulators as described above. They may also be used to screen further classes of candidate modulator, including antisense oligonucleotides. Such oligonucleotides are typically from 12 to 25, e.g. about 15 to 20 nucleotides in length, and may include or consist of modified backbone structures, e.g. methylphosphonate and phosphorothioate backbones, to help stabilise the oligonucleotide. The antisense oligonucleotides may be derived from the coding region of a target gene or be from the 5′ or 3′ untranslated region. Candidate molecules may further include RNAi, i.e. short double stranded RNA molecules which are sequence specific for a gene transcript, or a longer RNA sequence which can be processed by the cell into siRNA, and which can be provided to the cell e.g., as a DNA sequence (eliRNA, or expressed long interfering RNA). They may also include ribozymes which specifically target the transcript mRNA, i.e., a catalytic RNA molecule which cleaves other RNA molecules of a particular nucleic acid sequence. General methods for the construction of ribozymes are known in the art.

In a preferred embodiment of these aspects of the invention, the assay methods described above are used to determine modulators of activity of a protein or level of a transcript from Table 1b.

Modulators obtained in accordance with these aspects of the present invention may be used in methods of modulating tissue

inflammatory responses and/or conditions associated therewith, e.g., inflammatory conditions, in a patient.

The present invention therefore also provides a pharmaceutical composition comprising a modulator of a tissue inflammatory response and/or a condition associated therewith together with a pharmaceutically acceptable carrier therefor.

Generally, the modulator will be formulated with one or more pharmaceutically acceptable carriers suitable for a chosen route of administration to a subject. For solid compositions, conventional non-toxic solid carriers include, for example, pharmaceutical grades of mannitol, lactose, cellulose, cellulose derivatives, starch, magnesium stearate, sodium saccharin, talcum, glucose, sucrose, magnesium carbonate, and the like may be used. Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, etc, a modulator and optional pharmaceutical adjuvants in a carrier, such as, for example, water, saline aqueous dextrose, glycerol, ethanol, and the like, to thereby form a solution or suspension. If desired, the pharmaceutical composition to be administered may also contain minor amounts of non-toxic auxiliary substances such as wetting or emulsifying agents, pH buffering agents and the like, for example, sodium acetate, sorbitan monolaurate, triethanolamine sodium acetate, sorbitan monolaurate, triethanolamine oleate, etc. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, Pennsylvania, 15th Edition, 1975. The composition or formulation to be administered will, in any event, contain a quantity of the active compound(s) in an amount effective to alleviate the symptoms of the subject being treated.

Routes of administration may depend upon the precise condition being treated, though since endothelial cells form the lining of the vasculature, administration into the blood stream (e.g. by i.v. injection) is one possible route.

In addition, the present invention provides a modulator of a tissue inflammatory response and/or a condition associated therewith for use in therapy.

Furthermore, the present invention provides the use of a modulator of a tissue inflammatory response in the manufacture of a medicament for the treatment of a condition associated with said response.

Vectors

The identification of a number of ESTs and other genes of previously unknown function associated with regulation of endothelial cells by inflammatory signals provides the basis for novel vector systems useful in aspects of the invention described above, as well as further aspects described herein below.

Preferably, the sequence encoding a transcript listed in Table 1b is operably linked to a control sequence which is capable of providing for expression of the coding sequence by a host cell, i.e., the vector is an expression vector.

The term "operably linked" refers to a juxtaposition wherein the components described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under condition compatible with the control sequences.

Suitable host cells include bacteria, eukaryotic cells such as mammalian and yeast, and baculovirus systems. Mammalian cell lines available in the art for expression of a heterologous polypeptide include Chinese hamster ovary cells, HeLa cells, baby hamster kidney cells, COS cells and many others.

The vectors may include other sequences such as promoters or enhancers to drive the expression of the inserted nucleic acid, nucleic acid sequences so that the polypeptide is produced as a fusion and/or nucleic acid encoding secretion signals so that the polypeptide produced in the host cell is secreted from the cell.

The vectors may contain one or more selectable marker genes, for example an ampicillin resistance gene in the case of a bacterial plasmid or a neomycin resistance gene for a mammalian vector.

Vectors may further include enhancer sequences, terminator fragments, polyadenylation sequences and other sequences as appropriate.

Vectors may be used *in vitro*, for example for the production of RNA or used to transfect or transform a host cell. The vector may also be adapted to be used *in vivo*, for example in methods of gene therapy. Systems for cloning and expression of a polypeptide in a variety of different host cells are well known. Vectors include gene therapy vectors, for example vectors based on adenovirus, adeno-associated virus, retrovirus (such as HIV or MLV) or alpha virus vectors.

Promoters and other expression regulation signals may be selected to be compatible with the host cell for which the

expression vector is designed. For example, yeast promoters include *S. cerevisiae* GAL4 and ADH promoters, *S. pombe* nmt1 and adh promoter. Mammalian promoters include the metallothionein promoter which is can be included in response to heavy metals such as cadmium. Viral promoters such as the SV40 large T antigen promoter or adenovirus promoters may also be used. All these promoters are readily available in the art.

Vectors for production of polypeptides encoded by a transcript of Table 1b for use in gene therapy include vectors which carry a mini-gene sequence.

Vectors may be transformed into a suitable host cell as described above to provide for expression of a polypeptide of the invention. Thus, in a further aspect the invention provides a process for preparing polypeptides encoded by a transcript of Table 1b which comprises cultivating a host cell transformed or transfected with an expression vector as described above under conditions to provide for expression by the vector of a coding sequence encoding the polypeptides, and recovering the expressed polypeptides. Polypeptides may also be expressed using in vitro systems, such as reticulocyte lysate.

Polypeptides or fragments thereof in substantially isolated form encoded by an EST or gene of Table 1b form a further aspect of the present invention. Fragments of the polypeptides will preferably be at least 20 amino acids in size, and preferably from 25 amino acids up to the full length of the polypeptide.

A further aspect of the invention is nucleic acid sequences which encode said polypeptides and fragments thereof. Such

nucleic acid sequences may be included in vectors such as those described above.

For further details see, for example, Molecular Cloning: a Laboratory Manual: 2nd edition, Sambrook et al., 1989, Cold Spring Harbor Laboratory Press. Many known techniques and protocols for manipulation of nucleic acid, for example in preparation of nucleic acid constructs, mutagenesis, sequencing, introduction of DNA into cells and gene expression, and analysis of proteins, are described in detail in Current Protocols in Molecular Biology, Ausubel et al. eds., John Wiley & Sons, 1992.

Where a gene or EST of Table 1b is present in a vector, it may be linked in-frame to a translational initiation region for translation of said sequence, or alternatively it may be in an anti-sense orientation for transcription of anti-sense RNA.

Examples

TNFα, IL-1β and Interleukin-8 regulate transcript abundance

To allow a study of the effect of TNFα, IL-1β and Interleukin-8 on transcript abundance, seven independent primary cultures of HUVEC were cultured with a mixture of 15ng/mL of each of TNF-α, Interleukin-1β and Interleukin 8 for 24 hours. The RNAs extracted from these cultures were then used to prepare complex cRNA probes, which were hybridised to an Affymetrix U95A genechip (a 12,600-element Affymetrix gene array chip).

Analysis of Gene Chip Data

Transcript abundance data ("average differences") were globally scaled to bring the median gene expression of each chip (excluding control genes) to 1. To ensure transcript expression levels were comparable between arrays, the "LOESS"

function of the "R" statistical software system was applied to the log transformed average difference values of each array in comparison to a control array. The control array chosen was that which bore the closest similarity to the other six controls by Euclidean distance.

Normalised transcript abundance data was then compared using the CyberT algorithm (version 7.03; sliding window=301, Bayes estimate=21). This algorithm is an unpaired T-test, modified by the inclusion of a Baysian prior based on the variance of the other transcripts in the data set (Long *et al*, 2001, J. Biol Chem 276, 19937-19944).

For further statistical analysis, the "R" statistical software system and GeneSpring Expression Analysis Software (Silicon Genetics, Redwood City, Ca), were used.

Individual transcripts were categorised according to the functions of the proteins they encoded, using the GO database (www.geneontology.org), Entrez (www.ncbi.nlm.nih.gov/entrez) or OMIM (www.ncbi.nlm.nih.gov:80/entrez/Omim) databases.

In the Tables, fold changes are expressed as unpaired means over the seven experiments (i.e., mean of inflammatory treated/mean of control).

Difference in transcript levels in different endothelial cell types

To determine whether the modulation of the transcriptome is comparable amongst different endothelial cell types, we obtained a further culture using one each of human coronary artery endothelial cells (HCAEC) and human uterine microvascular endothelial cells (UtMVEC).

The three different cell types were treated with inflammatory signals as above, and the extent to which the transcript abundance is regulated in each of the three cell types was assessed. A pattern of regulation between the three cell types was also determined. It was found that most transcripts are regulated in all three cell types, while some are regulated in only two or only one of these cell types.

Those transcripts which are regulated in all three cell types are believed to be particularly useful in the various methods of the present invention, since they are likely to be meaningful in a variety of inflammatory conditions affecting distinct organs.

Moreover, it was also found that the transcripts which are modulated by inflammatory signals in all three endothelial cell types tend also to be strongly modulated by inflammatory signals in HUVEC.

Consensus data

Table 1a and 1b show a consensus set of transcripts. These were selected on the basis that their level before and after treatment with inflammatory mediators differs by a factor of two or more (in either direction), with a Baysian P value of less than 0.001. These have been grouped according to gene family.

Table 1 shows the extent of regulation in HUVEC cells, and also in HCAEC and UtMVEC cells.

ESTs

A number of ESTs and genes of previously unknown function identified as relevant to the present invention are of particular interest in the various methods of the invention

and as possible therapeutics for use in treatments. These are summarised in Table 1b. The specific sequences of the probes used to isolate these ESTs are shown in Table 2b.

Materials and Methods:

Preparation of endothelial cells

HUVECs isolated from seven different individuals were cultured in Microvascular Endothelial Cell Growth Medium-2 (EBM-MV, Biowhittaker). Medium was supplemented with a proprietary mixture of human Epidermal Growth Factor, Hydrocortisone, Vascular Endothelial Growth Factor, human Fibroblast Growth Factor, human recombinant Insulin-like Growth Factor, Ascorbic Acid, Gentamicin, Amphotericin-B and FBS (5%) (Microvascular Bulletkit™ reagents, Biowhittaker. At passage 5, each HUVEC isolate was divided between two 175cm^2 culture flasks and grown to 70% confluence. For each HUVEC isolate, growth medium in one flask was replaced with fresh medium containing a cocktail of 15 ng each IL-8, IL-1β and TNF-α. As a control, medium in replicate cultures was replaced with fresh medium only. Cytokine-treated HUVECs and controls were cultured for a further 24 hrs

Single donor-derived human coronary artery ECs and uterine myometrial microvascular ECs were purchased from Biowhittaker. Cells were cultured and treated under identical conditions as HUVECs

RNA Extraction

RNA was extracted from each culture using Trizol reagent (Gibco/BRL, UK), followed by a clean up through an RNeasy™ spin column (Qiagen, UK) and ethanol precipitation. RNA integrity was assessed using an Aligent 2100 bioanalyser.

Analysis of RNA

Biotinylated target cRNA was prepared according to Affymetrix protocol, hybridised to Affymetrix human U95Av2 chips and globally scaled using Microarray Suite Version 4.0 or 5.0 software.

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Table 1a. Transcripts regulated by inflammatory mediators

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
265_s_at	ELAM-1	6401	94.12407276	0	52.80610911	48.1406623
38453_at	ICAM-2	3384	-4.919652169	0	-3.172225055	-4.196639495
38454_g_at	ICAM-2	3384	-4.273813746	6.85E-14	-3.222848571	-4.756558142
41433_at	VCAM-1	7412	41.92536277	4.44E-16	19.68500876	7.08367969
590_at	ICAM-2	3384	-4.355207383	0	-2.939770867	-3.513733465
32640_at	ICAM-1	3383	30.3312002	0	22.98537954	17.77124304
1372_at	TNF-induced protein 6 (high homology to CD44)	7130	72.77639371	2.64E-12	102.0554489	132.4555661
583_s_at	VCAM-1	7412	21.72229281	4.54E-14	12.47672759	8.084337024
37286_at	Neuronal CAM	4897	3.057294936	2.6E-11	4.522694277	3.046878985
37287_at	Neuronal CAM	4897	2.118308598	0.00016866	3.028078666	1.459527209
1126_s_at	CD44	---	5.908575047	1.69E-10	5.164794759	4.433329962
2036_s_at	CD44	960	5.280337829	4.8E-10	4.346849483	4.014976193
31472_s_at	CD44	---	5.028849347	1.41E-10	5.268492975	3.537170724
41475_at	Ninjurin 1	4814	4.254200441	1.25E-12	8.697922867	2.140258321
1385_at	TGF beta induced gene big-h3 (inhibits cell adhesion)	7045	3.148463542	4.32E-08	2.554804325	5.017906407
40493_at	CD44	960	2.314611255	0.000015	2.992670691	2.618091422
41534_at	Protocadherin (brain-heart)	5099	-3.130162659	5.24E-11	-3.950798183	-1.443373336
37288_g_at	Neuronal CAM	4897	2.32386108	0.00000712	3.096319968	2.468852275
41266_at	integrin, alpha 6	3655	-2.905539743	6.34E-14	-6.443317073	-4.825692909
33410_at	Integrin alpha 6B	3655	-3.555248053	5.49E-11	-3.460672051	-7.074752389
33411_g_at	Integrin alpha 6B	3655	-4.026330886	1.62E-08	-7.112851076	-10.75631742
120_at	Integrin alpha 1	3672	5.394552373	5.46E-11	8.278974088	15.79277269
37484_at	integrin, alpha 1	3672	7.015160862	2.69E-09	15.12333177	12.4415517
257_at	Integrin alpha V	3685	2.327640731	0.00028556	1.203881437	3.677134895
39071_at	Integrin alpha V	3685	4.093727059	1.11E-15	2.057183486	4.695101368
406_at	Integrin, beta 4	3691	-2.516147583	0.0000113	-1.175618714	1.170070754
2073_s_at	cadherin 13, H-cadherin (heart)	1012	2.169729435	0.00074496	1.053001021	1.209382473
39878_at	protocadherin 9	5101	-4.59180328	0.00000262	-4.173958272	-1.224867651
34760_at	C-type lectin BIMLEC precursor	9936	-2.931920451	0.0004342	-2.84198351	-3.951644147
40698_at	C-type lectin,	9976	-2.090795467	0.0000308	-1.170337293	-1.25139979
Apoptosis regulation						
1717_s_at	IAP1	330	13.25120688	2.22E-16	24.06057001	10.88814977
595_at	TNF-inducible A20	7128	23.99969733	0	24.66171353	36.22756341
41384_at	RIPK2 (interacts with CD40)	8767	33.39955874	0	10.50930817	27.65190479
33243_at	TNF-induced protein (? negative mediator of apoptosis)	25816	4.48308487	3.44E-15	5.510033362	5.437586371
1237_at	immediate early response 3	8870	2.804193654	3.02E-13	3.090900931	7.298832868
1867_at	CLARP	8837	2.893895437	2.76E-12	2.965378608	2.598032615
36578_at	MIHB (IAP homologue)	329	2.20726532	6.59E-10	1.998610122	2.184746309
1868_g_at	CLARP	8837	2.741709407	2.77E-12	1.892992274	2.014557756
40049_at	death-associated protein kinase 1	1612	-2.30278615	2.27E-07	-3.336581791	-2.887251828

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
41816_at	caspase recruitment domain family, member 10	29775	-2.002003766	3.91E-08	-2.186735523	-2.029925561
2002_s_at	BCL2-related protein A1	597	2.613589324	0.00018672	3.9139111	1.474571201
574_s_at	caspase 1 (interleukin 1, beta, convertase)	834	3.488039515	0.0000158	5.206924741	2.289334595
Proteases						
1006_at	MMP 10 (stromelysin)	4319	20.673524	2.94E-09	54.6446216	12.16240346
1227_g_at	disintegrin/metalloproteinase domain 17 (TNF-alpha converting enzyme)	6868	3.813351746	5.27E-09	1.452030457	5.668869009
129_g_at	cathepsin K (pycnodysostosis)	1513	2.462139973	0.00000177	1.72558228	2.194661317
38466_at	cathepsin K (pycnodysostosis)	1513	3.61266368	3.93E-10	2.466729636	1.611499
128_at	cathepsin K (pycnodysostosis)	1513	5.727765674	3.54E-07	2.95658194	1.862569449
41239_r_at	cathepsin S	1520	6.178963194	0.00010333	8.40720437	7.301525957
Growth factors/Growth factor receptors/binding proteins						
1736_at	insulin-like growth factor binding protein 6	3489	-2.014	0.0147	-1.977	-6.608
34021_at	interleukin 2	3558	-3.214	0.0041	1.1863	-1.027
36782_s_at	insulin-like growth factor 2 (somatomedin A)	3481	2.9966	0.0197	1.0001	-1
37319_at	insulin-like growth factor binding protein 3	3486	-2.874	0.0035	-3.36	-1.027
159_at	VEGF C	7424	2.357296176	2.67E-10	9.487520679	2.865003832
37461_at	anglopoletin 2	285	-2.319743262	0.00000274	-5.975448459	-7.930241469
1951_at	angiopoietin 2	285	-2.685484753	4.54E-07	-8.039282583	-12.53026423
36879_at	endothelial cell growth factor 1 (platelet-derived)	1890	9.066420458	9.88E-09	23.27852668	1.656563558
1334_s_at	colony stimulating factor 3 (granulocyte)	1440	110.4374129	0	107.7019762	95.9009041
1400_at	colony stimulating factor 2 (granulocyte-macrophage)	1437	59.85609631	0	128.3173278	115.0807894
1401_g_at	colony stimulating factor 2 (granulocyte-macrophage)	1437	69.22778507	0	164.8742173	97.00671055
39781_at	IGFBP4	3487	-2.32298013	2.63E-12	-3.202031547	-2.304705004
1573_at	platelet-derived growth factor beta polypeptide	5155	2.364292483	4.72E-11	2.310014432	3.576039834
1737_s_at	IGFBP4	3487	-3.134319307	3.56E-11	-4.670559679	-2.390794223
1987_at	platelet-derived growth factor receptor, alpha polypeptide	5156	5.414971705	2.1E-10	5.239961839	5.489227387
1897_at	transforming growth factor, beta receptor III	7049	-3.075084973	0.00000944	-2.117136032	-6.575991342
1761_at	platelet-derived growth factor receptor-like	5157	2.189929847	0.0000242	1.689699835	-1.658417287
1968_g_at	platelet-derived growth factor receptor, alpha polypeptide	5156	3.489609752	0.00017615	7.37795097	3.825705997
36314_at	fms-related tyrosine kinase 3 ligand	2323	2.928004872	4.78E-07	4.061156781	1.381073451
1664_at	Insulin-Like Growth Factor 2	---	2.468425254	1.35E-07	1.028272127	1.071858187
1591_s_at	insulin-like growth factor 2	3481	4.554886105	0.000025	2.380846497	-1.095495947

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
Bone morphogenetic proteins						
40333_at	BMP4	652	-8.689531567	2.23E-11	-11.51217679	-13.66978546
1114_at	BMP4	652	-5.224251224	1.06E-10	-8.834024069	-3.466831976
1113_at	BMP2	650	4.225472624	5.05E-10	5.016446479	10.99944132
40367_at	BMP-2A	650	3.76567886	2.92E-09	5.685709393	9.647738498
Cell Signalling						
849_g_at	TRAF1	7185	17.5138547	0	8.878582574	11.87121514
848_at	TRAF1(signal transduction)	7185	7.479968747	0	7.120389129	7.914739757
1633_g_at	pim-2 oncogene (serine threonine kinase)	11040	9.160464547	0	14.689145	15.21104429
32737_at	Rac2 (small GTP binding protein)	5880	3.658480457	3.89E-15	2.744061787	1.789830328
38433_at	AXL receptor tyrosine kinase	558	-2.808585886	1.27E-13	-3.296941327	-2.913417469
32736_at	ras-related C3 botulinum toxin substrate 2	28963	2.682083886	4.5E-13	1.753959656	1.421575242
962_at	BMX non-receptor tyrosine kinase	660	-2.535033842	2.24E-10	-2.901079423	-3.416983113
1278_at	Tyrosine Kinase, Receptor Axl, Alt. Splice 2	---	-2.419620683	1.58E-12	-2.432209903	-3.146520458
35666_at	semaphorin 3F	6405	-2.323822657	1.19E-11	-3.747425517	-3.105083997
41592_at	JAK binding protein	8651	15.5029436	4.44E-16	13.24058381	18.69333246
37745_s_at	suppression of tumorigenicity 5 (regulates MAPK1/ERK2 kinase)	6764	3.798748042	8.78E-12	1.673006765	3.978556319
35414_s_at	jagged 1	182	3.938751608	3.97E-10	1.916173689	3.913844547
38129_at	glycerol kinase	2710	4.156535178	2.03E-11	4.389062428	4.783183323
33925_at	neurogranin (protein kinase C substrate)	4900	-2.874103959	1.01E-09	-2.584237728	-2.07114957
37637_at	regulator of G-protein signalling 3	5998	2.316785124	1.21E-09	2.467991159	3.293642315
32616_at	v-yes-1	4067	3.430788342	7.13E-11	2.724701376	1.854721285
1402_at	V-yes-1 homolog, Lyn (tyrosine kinase)	4067	3.523004339	1.58E-08	2.854373847	1.829548828
37701_at	regulator of G-protein signalling 2 (negative regulator)	5997	2.813879055	2.08E-08	3.885900214	3.315667451
36215_at	protein kinase, cAMP-dependent, catalytic, beta	5567	-2.628783273	1.51E-08	-3.752926478	-6.755566769
1674_at	v-yes-1 homolog 1	7525	-2.152710145	3.31E-08	-1.530253982	-2.804444302
36233_at	3'-phosphoadenosine 5'-phosphosulfate synthase 2	9060	2.027727485	4.72E-08	1.510192698	-1.077558923
38130_s_at	glycerol kinase (testis specific)	---	7.973762615	2.5E-09	8.684790212	2.068851547
1788_s_at	dual specificity phosphatase 4 (negatively regulates MAP kinases)	1846	-11.76290841	7.65E-07	-2.071776576	-3.485764407
1637_at	MAPKAP kinase 3	7867	-2.182787462	0.00000659	-2.402844278	-4.904366595
34273_at	regulator of G-protein signalling 4	---	-2.496810967	2.85E-07	-4.377804301	-9.38699972
34272_at	regulator of G-protein signalling 4	5999	-3.344620441	9.24E-09	-6.561315389	-16.14378204
1652_at	pim-2 oncogene (serine threonine kinase)	11040	2.699937536	1.09E-09	3.836282227	4.323718343
31862_at	Wnt 5A	7474	4.219642672	0.0000149	-1.366311375	1.011983622

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
1669_at	Wnt-5a	7474	3.479040912	0.00069919	-1.444116368	1.01235564
1457_at	JAK 1	3716	2.045332134	6.78E-08	1.365238795	1.006354866
1845_at	MAP kinase kinase 4	6416	2.521474928	0.00063222	2.41305386	-1.836490086
40648_at	c-mer proto-oncogene tyrosine kinase	10461	-2.063640257	0.0000592	-2.378445569	-2.262491022
38880_at	likely ortholog of mouse mitogen activated protein kinase binding proten 1	23005	2.215609357	4.77E-09	1.944472584	1.888827336
2014_s_at	mitogen-activated protein kinase kinase 6	5608	-2.618846506	0.00012111	-2.956702088	-5.484778343
1223_at	PCTAIRE protein kinase 3	5129	2.680986947	0.00064597	2.263745506	1.108537941
37221_at	protein kinase, cAMP-dependent, regulatory, type II, beta	5577	-2.08567496	0.00000622	-2.915269541	-2.071588434
2024_s_at	v-yes-1	4067	2.379576108	1.34E-08	2.920175571	1.392260421
323_at	Serine Kinase Psk-H1	---	-2.016724782	0.0000125	-1.359560601	-1.12682497
481_at	SNF-1 related kinase	54861	-2.583587042	0.00000144	-1.719525409	-2.586396156
Cytokines/Chemokines						
431_at	chemokine (C-X-C motif) ligand 10	3627	2.8162	0.0131	21.833	6.9624
35061_at	chemokine (C-X-C motif) ligand 11	6373	2.1907	0.0158	19.314	6.2232
36444_s_at	chemokine (C-C motif) ligand 23	6368	-4.887	0.001	-2.116	-1.418
38299_at	IL6	3569	24.14721637	0	22.56841253	61.56303356
35372_r_at	IL8	3576	15.51735527	0	15.55547961	12.15835237
1369_s_at	IL8	---	41.62876467	0	22.98760049	12.09571155
34022_at	Gro-gamma	2921	48.02792301	0	73.86427422	86.20366678
35410_at	granulocyte chemotactic protein 2	6372	121.6423946	0	114.3849865	29.67507825
40385_at	Exodus-1 (MIP-3 alpha)	6364	82.45859231	0	189.9224072	106.6857086
34375_at	MCP-1	---	14.29518512	0	3.308055282	11.6027416
875_g_at	MCP-1	6347	10.76460673	0	3.43922774	8.863220251
37187_at	Gro-beta	2920	39.20393321	0	14.16208753	39.61686592
408_at	Gro-alpha	---	23.14045021	0	6.291677693	7.986953794
35025_at	ENA-78 (neutrophil activation)	6374	11.02707172	4.25E-10	9.840379417	41.69374269
874_at	MCP-1	6347	5.836636513	2.11E-15	4.481375208	9.794572686
1520_s_at	IL-1 beta	3553	91.84552248	8.47E-13	205.4748788	177.3630307
33849_at	pre-B-cell colony-enhancing factor	10135	3.813578354	3.97E-10	4.108018493	4.081292457
39402_at	IL-1 beta	3553	31.54329146	3.09E-13	82.81268573	85.84762636
823_at	fractalkine	6376	17.68369443	2.56E-12	19.7422482	22.71709814
33790_at	small inducible cytokine A15	6358	-12.67742209	1.52E-08	-48.34300032	-66.0221188
1403_s_at	small inducible cytokine A5 (RANTES)	6352	11.20684756	5.42E-07	37.22680311	12.48514714
1405_i_at	small inducible cytokine A5 (RANTES)	6352	85.06201489	0.00049761	72.24870591	43.38032562
38488_s_at	IL15	3600	2.963696814	0.00000871	4.781012455	3.292355333
36445_at	chemokine (C-C motif) ligand 23	6368	-3.602748819	0.00039698	-2.406722814	-1.030688433
37823_at	chemokine (C-C motif) ligand 8	6355	23.02933617	0.00052146	258.0717884	125.0305056
37712_g_at	Myocyte enhancer-binding factor 2; MEF2	---	-4.26612691	2.43E-07	-5.003135162	-6.008429791
37565_at	monocyte to macrophage	23531	2.119735439	0.0000216	1.403749822	1.977961258

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
	differentiation-associated					
Cytokine/Chemokine Receptors						
1370_at	IL7 receptor	3575	9.161091199	0	4.303383875	8.240362396
36227_at	IL7 receptor	3575	18.86860288	0	21.47752128	19.22542292
40322_at	interleukin 1 receptor-like 1	9173	2.413606464	4.3E-14	3.10203053	1.491371089
36377_at	interleukin 18 receptor 1	8809	4.044516303	2.99E-11	5.074365709	3.86178169
37493_at	colony stimulating factor 2 receptor, beta	1439	3.657465472	5.4E-11	4.215999509	4.372152437
41677_at	IL 15 receptor alpha	3601	2.771385255	3.93E-09	6.171752712	4.132002608
40310_at	toll/interleukin 1 receptor-like 4	7097	17.04231159	6.34E-08	41.69446428	92.69458196
1061_at	interleukin 10 receptor, alpha	3587	2.396040273	0.00025159	1.656307749	2.726745302
1086_at	colony stimulating factor 2 receptor, beta, low-affinity	1439	3.132593874	0.00070665	3.024617357	-1.320929175
37494_at	colony stimulating factor 2 receptor, beta, low-affinity	1439	2.857904787	0.00000274	4.308632923	1.561972298
Transcriptional regulation						
1052_s_at	CCAAT/enhancer binding protein, delta (COX-2 promoter regulation)	1052	11.91692976	0	11.83059529	10.65191899
2049_s_at	jun B	3726	5.153898931	1.81E-14	3.431192771	6.223449667
1461_at	MAD-3 (encoding I-kappa-B activity)	4792	10.50494004	0	8.003192106	5.490720521
38438_at	NF kappa B (p105)	4790	4.04722666	0	4.805775558	3.759579948
545_g_at	NF kappa B (p50)	4791	4.794779209	7.11E-15	9.451858522	5.944229815
1377_at	NF kappa B (p105)	4790	4.434308127	0	3.02369062	3.934373217
1378_g_at	NF kappa B (p105)	4790	5.534025442	1.11E-16	7.587979568	5.198094808
669_s_at	interferon regulatory factor 1	3659	7.50488352	1.73E-14	7.563755727	4.851132396
40362_at	NF kappa B 2 (p49/p100)	4791	5.793454912	1.11E-16	7.300267454	7.131728502
35724_at	Pirin (transcription co-factor)	8544	-3.930125583	6.44E-15	-4.412262675	-4.67615839
32786_at	jun B	3726	3.920893987	5.77E-12	2.207915162	3.564535817
31895_at	basic leucine zipper transcription factor 1	571	4.475370873	1.25E-14	5.111364686	4.25002483
570_at	RELB (inhibits NF kappa B)	5971	3.894337906	9.21E-15	3.223675004	3.270575768
40088_at	nuclear receptor interacting protein 1	8204	3.771630231	1.19E-13	4.396979347	3.998851735
37353_g_at	nuclear antigen Sp100 (stimulates transcriptional activity of Ets-1)	6672	2.880868474	1.02E-10	2.394226199	2.256154686
35638_at	core-binding factor,alpha subunit 2; cyclin D-related	862	-4.316374281	5.68E-13	-4.593414984	-2.069158236
34720_at	nuclear factor I/B	4781	-2.891380748	9.37E-12	-5.585236612	-6.207114141
36057_at	armadillo repeat protein ALEX2	9823	3.105240733	1.54E-11	1.835928633	2.175918631
544_at	NF kappa B (p50)	4791	7.587736834	4.66E-15	10.21368896	6.96686111
38944_at	MAD-3 homolog	4088	2.544980211	2.89E-11	2.527083313	1.211400339
41743_i_at	transcription factor IIIA-interacting protein (TNF-inducible)	10133	3.2823426	8.83E-12	2.335070811	1.505620716
37352_at	nuclear antigen Sp100 (stimulates transcriptional	6672	3.210793569	1.98E-11	2.197590225	2.387759855

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
	activity of Ets-1)					
1433_g_at	MAD-3	4088	2.098641883	8.83E-09	1.666043623	1.27364714
41742_s_at	transcription factor IIIA-interacting protein (TNF-inducible)	10133	3.401140074	4.64E-13	2.930879849	1.665969002
36825_at	stimulated trans-acting factor (50 kDa), repressor of viral transcription	10346	2.40612763	7.67E-09	1.625963386	1.795469106
32588_s_at	EGF-response factor 2	678	-2.246354328	4.4E-09	-3.889915623	-3.550964514
40091_at	bcl-6 (transcriptional repressor)	604	3.560324596	2.07E-10	4.016477251	4.918915862
32794_g_at	T cell receptor beta locus	6957	-4.582802536	1.56E-10	-6.335942518	-5.302631449
35844_at	syndecan 4 (intracellular communication)	6385	6.189681078	2.01E-10	9.509706352	7.651058689
205_g_at	homeo box A4	3201	2.867789963	1.07E-09	1.253183174	1.356465181
33281_at	IKK-related kinase epsilon	9641	3.036807944	1E-13	2.812228259	3.715110089
38276_at	I kappa B epsilon	4794	2.587016943	4E-10	3.454608864	1.573492134
463_g_at	nuclear factor I/B	4781	-3.326218015	3.38E-09	-2.789337322	-2.93715476
40511_at	GATA-binding protein 3 (T-cell antigen regulation)	2625	-3.077856942	1.74E-09	-2.214428235	-1.15998505
1102_s_at	glucocorticoid receptor alpha	2908	2.639244551	0.00000028	3.1698879	2.569716707
873_at	homeo box A5	---	2.56550767	5.85E-07	1.169613734	1.194134559
32168_s_at	Down syndrome critical region gene 1	1827	2.21618204	0.0000103	2.997097995	1.558897138
40493_at	zinc finger protein 6 (CMPX1), function unknown	960	2.314611255	0.000015	2.992670691	2.618091422
40393_at	homeo box A4	3201	4.225364843	1.13E-10	1.732294373	1.372777345
39742_at	TRAF-interacting factor	10010	2.142165615	0.0000156	1.785436095	2.694870743
33113_at	Cbp/p300-interacting transactivator	10370	-2.08039694	6.98E-08	-1.710148426	-2.094438928
204_at	homeo box A4	3201	6.799784725	3.76E-12	2.135352044	1.228357243
38439_at	nuclear factor-like 1 (? ferritin gene expression)	4779	2.105432331	1.08E-10	1.731916025	2.233679314
35992_at	musculin (transcriptional repressor)	9242	4.59261857	1.66E-07	5.0459609	9.910746814
38278_at	modulator recognition factor I	10865	2.090810626	1.95E-07	1.797705792	1.362064745
1577_at	androgen receptor	367	-2.998677788	2.74E-07	1.084402729	-2.024294255
33439_at	transcription factor 8 (represses IL-2 expression)	6935	2.463550746	1.13E-07	1.432420689	2.276427567
36690_at	Glucocorticoid receptor, lymphocyte	2908	2.202243881	3.5E-08	1.694016378	1.871546701
39032_at	TGF beta stimulated protein (regulates C-type natriuretic peptide gene)	8848	-2.226498199	2.04E-07	-2.979839304	-1.851582699
32034_at	Kruppel-like transcription factor	7764	2.247161582	9.04E-07	2.1386648	1.611108294
287_at	activating transcription factor 3	467	4.037944598	0.00021361	5.867934682	2.449017154
37419_g_at	POU domain, class 2, transcription factor 2	5452	3.570311319	8.54E-07	10.2030961	7.279581414
37417_at	POU domain, class 2, transcription factor 2	5452	3.15917466	1.82E-09	6.743320713	3.658601746
943_at	runt-related transcription factor 1	861	3.123404286	3.88E-11	2.595679083	2.208405598
393_s_at	runt-related transcription factor 1	861	2.718511505	5.28E-07	2.094702547	1.753450444

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
39421_at	runt-related transcription factor 1	861	2.330472883	1.54E-08	2.842674795	1.989573274
535_s_at	NF-kappa B 2 (p49/p100)	4791	7.014437801	8.77E-09	12.09195342	6.581215622
40823_s_at	transcription factor NFATx4	4775	-2.078620759	0.00095663	-1.45270611	-1.629367546
33130_at	homeo box D1	3231	-5.00861908	3.68E-08	-2.579094814	-5.352803906
35824_at	zinc finger protein 238	10472	-2.383931066	6.72E-07	-4.13316475	-3.964515214
32034_at	zinc finger protein 217	7764	2.247161582	9.04E-07	2.1386648	1.611108294
39681_at	zinc finger protein 145 (Kruppel-like)	7704	2.477517897	0.00000829	1.736511126	1.220799652
41612_at	zinc finger protein 264	9422	4.296329969	0.0000447	-1.079860264	-6.156102305
39633_at	S100 calcium binding protein A3	6274	2.829339235	0.00036814	12.49571209	5.162186098
40126_at	paired mesoderm homeo box 1	5396	3.283107586	0.00034973	10.49393725	6.156341582
40199_at	msh homeo box homolog 1 (Drosophila)	4487	2.409909357	0.0000071	2.521903121	2.708781174
215_g_at	msh homeo box homolog 1 (Drosophila)	4487	2.329390033	0.0002391	3.803589095	7.060846295
Enzymes						
34304_s_at	spermidine N1-acetyltransferase (polyamine catabolism)	6303	6.704420999	6.44E-15	3.431292345	4.27011499
1173_g_at	spermidine/spermine N1-Acetyltransferase, Alt. Splice 2	---	4.132527389	0	2.917946858	3.523924496
1069_at	COX-2	---	34.72962658	0	60.94542155	124.409157
33862_at	phosphatidic acid phosphatase type 2B	8613	3.214894884	2.78E-13	3.604930643	3.689974385
34666_at	Mn SOD	6648	21.14199305	0	41.56950623	36.7453472
39640_at	glutamine-fructose-6-phosphate transaminase 2 (hexosamine biosynthesis)	9945	5.640667138	2.42E-14	5.982698011	8.612059352
40215_at	UDP-glucose ceramide glucosyltransferase	7357	4.897679713	0	3.893723735	4.931113889
41352_at	beta-galactoside alpha-2,6-sialyltransferase (glycosylation)	6480	5.993191486	0	3.047035442	4.933917672
34390_at	proline 4-hydroxylase, alpha polypeptide II	8974	3.99041836	5.55E-16	5.868560288	4.278419323
40290_f_at	beta-galactosidase alpha-2,3-sialytransferase (glycosylation)	6482	6.686428065	9.24E-12	4.85511756	2.420407432
576_at	NO synthase	4846	-10.63785461	0	-13.32725039	-5.923096431
37402_at	Rnase 1, pancreatic	6035	-4.245955517	1.46E-10	-5.030206449	-6.634617447
38066_at	diaphorase (NADH/NADPH) (cytochrome b-5 reductase)	1728	-2.415151638	6.38E-09	-1.305264298	-3.114333412
36658_at	3-beta-hydroxysterol delta-24-reductase (cholesterol biosynthesis)	1718	-2.643697649	9.12E-12	-2.593239368	-3.836044468
40568_at	ATPase, H+ transporting, lysosomal	526	2.371659873	4.34E-11	3.185827679	2.637705921
33707_at	Phosholipase A2 gamma (cytosolic)	8605	3.261679914	3.69E-11	3.522257814	2.301935515
34876_at	carboxypeptidase D	1362	3.076753085	1.94E-10	2.897736214	3.000177375
231_at	transglutaminase 2 (crosslinks proteins)	7052	-2.617617679	8.12E-14	-3.334570859	-2.678284178

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
35938_at	phospholipase A2 (cytosolic, calcium-dependent)	5321	3.619599149	3.8E-13	2.366489356	3.253061315
38129_at	glycerol kinase (metabolizes endogenous and dietary glycerol)	2710	4.156535178	2.03E-11	4.389062428	4.783183323
40671_g_at	L-kynurenine hydrolase (tryptophan metabolism)	8942	19.54992096	7.83E-13	31.92023266	35.93860554
41654_at	adenosine deaminase	100	2.826089391	3.24E-10	3.599789192	3.713396127
33802_at	Heme Oxygenase 1	3162	-3.426190665	1.24E-08	1.138813035	-3.346040419
37015_at	aldehyde dehydrogenase 1, soluble	216	-4.815533737	1.08E-13	-7.172622822	-5.357724575
36149_at	dihydropyrimidinase-like 3	1809	2.348831769	2.55E-10	1.790570365	2.165038959
32718_at	tyrosylprotein sulfotransferase 1 (modifies proteins in inflammation)	8460	2.226480677	3.24E-07	1.761306768	2.35714199
41656_at	N-myristoyltransferase 2	9397	-2.01967345	5.85E-09	-2.434231443	-3.519602144
1227_g_at	TNF alpha converting enzyme	6868	3.813351746	5.27E-09	1.452030457	5.668869009
41601_at	TNF alpha converting enzyme	6868	2.795464504	4.04E-09	1.860860363	2.545861043
39663_at	mannosidase, alpha, class 2A, member 1 (golgi enzyme)	4124	2.172987708	1.64E-09	2.83218502	2.310898922
37944_at	GTP cyclohydrolase 1 (dopa-responsive dystonia, NO synthesis)	2643	4.438893651	1.75E-09	14.75969444	8.812737944
40672_at	L-kynurenine hydrolase (involved in biosynthesis of nad cofactors)	8942	2.673122374	4.73E-10	3.563621638	4.441970617
38463_s_at	adenosine monophosphate deaminase, erythrocyte isoform	272	3.252956552	0.0000363	4.881773924	2.28032833
40505_at	ubiquitin-conjugating enzyme E2L 6	9246	2.260319502	0.00000441	6.11613235	1.848697939
38315_at	retinaldehyde dehydrogenase 2	8854	-3.141750466	8.22E-10	-1.56562427	-1.111060049
34261_at	phosphate cytidylyltransferase 2, ethanolamine	5833	-2.168441607	2.43E-07	-2.495275565	-3.137010475
1226_at	TNF alpha converting enzyme	6868	2.300272424	0.00000707	1.004340971	2.756217115
37255_at	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 2	8509	2.216017066	0.0000592	2.306019166	1.291774578
35396_at	hyaluronan synthase 2	3037	4.945257021	0.0000787	1.000129624	3.057807352
37608_g_at	ketohexokinase (fructokinase)	3795	-2.946029683	0.0000001	-2.552822874	-1.840790023
35702_at	hydroxysteroid (11-beta) dehydrogenase 1	3290	5.464059097	2.13E-07	4.384698173	7.735231534
1212_at	glutathione transferase zeta 1 (maleylacetoacetate isomerase)	2954	2.588622881	1.25E-07	1.930737369	1.42606759
39791_at	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	488	2.012343217	0.00000004	1.822188224	2.032942103
40214_at	UDP-glucose ceramide glucosyltransferase	7357	4.72644372	7.22E-09	3.814508262	4.080889627
41711_at	thioredoxin reductase 2	10587	-2.948650383	2.67E-08	-6.378914918	-8.72831537
35966_at	glutaminyl-peptide	25797	2.328202379	3.18E-08	2.329644161	2.391292262

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
	cyclotransferase (glutaminyl cyclase)					
32772_s_at	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 1	2683	4.456181198	0.0000175	1.238263347	1.497110144
39107_at	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	4047	3.358766219	0.00073095	1.390518246	1.534806813
34636_at	arachidonate 15-lipoxygenase	246	2.440589489	0.00067786	2.682402797	4.947969996
40670_at	kynureninase (L-kynurenine hydrolase)	8942	7.008740575	0.00043779	1.470999146	1.901287336
37841_at	butyrylcholinesterase	590	-4.246686347	0.0000456	1.724782943	-1.270228337
712_s_at	Serine Hydroxymethyltransferase, Cytosolic, Alt. Splice 3	---	-2.610161222	0.000031	-1.94665557	-2.625365856
34209_at	inositol 1,4,5-trisphosphate 3-kinase C	80271	2.90950996	0.00040388	3.289484052	-1.391614528
39267_at	phosphoglucomutase 3	5238	2.053010541	0.00000242	1.904710164	1.542414689
Cell cycle regulation						
37218_at	BTG3 (negative control of cell proliferation)	10950	2.624092795	2.45E-10	3.856424559	3.197893027
35153_at	P95 (nibrin)	4683	2.136226929	2.84E-09	2.994019488	2.441142021
425_at	P27	3429	2.762082411	3.66E-09	2.627038307	1.886894848
1207_at	cyclin-dependent kinase 6	1021	2.455451672	0.0000135	-1.062090681	1.219554564
40399_r_at	mesenchyme homeo box 2 (growth arrest-specific homeo box)	4223	-2.245407634	0.00018939	-1.677937769	1.360368999
38326_at	putative lymphocyte G0/G1 switch gene	50486	5.210351552	9.34E-07	4.501028149	2.835700322
Cell communication						
32531_at	Connexin 43	2697	2.368387646	2.65E-11	1.97846913	2.001682474
2018_at	Connexin 43	2697	3.031077047	1.69E-07	2.474557415	2.815825621
40687_at	gap junction protein, alpha 4, 37kDa (connexin 37)	2701	-5.56891197	0.0000116	-3.025458771	-2.091117495
Nuclear proteins						
37027_at	AHNAK nucleoprotein (desmoyokin)	195	-2.16666252	1.49E-09	-2.455018307	-3.26541786
286_at	H2A histone family, member O	8337	3.115339124	7.26E-09	4.90449378	3.960532543
37354_at	nuclear antigen Sp100	6672	3.058654921	1.07E-07	2.643890811	1.040688287
32609_at	H2A histone family, member O	8337	15.67613628	9.49E-10	13.14154378	5.736367488
39397_at	nuclear receptor subfamily 2, group F, member 2	7026	-2.044215909	1.98E-09	-2.272605283	-2.260646545
37377_i_at	lamin A/C (structural protein of nuclear envelope)	4000	-2.350943533	1.75E-10	-2.555422079	-1.767515468
33249_at	nuclear receptor subfamily 3, group C, member 2	4306	-2.584848636	3.41E-08	-1.739378234	-1.562212566
34690_at	SWI/SNF related subfamily c, member 2	6601	-2.088814752	0.00000536	-1.565957305	-1.282789174
32668_at	single-stranded DNA	23635	-3.149577521	0.00031465	-1.640548596	-2.145738917

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
	binding protein 2					
Cytoskeletal						
41439_at	myosin class I (mutated allele)	4430	9.740468685	2.06E-10	14.70291906	10.25673133
33102_at	adducin 3 (gamma)	120	3.391355995	1.1E-12	6.424336776	3.508692997
34082_at	slingshot 1 (F-actin binding)	54434	2.484987537	2.07E-10	1.636955316	1.21353576
36792_at	tropomyosin 1 (alpha)	7168	2.572958966	2.38E-11	1.214714872	1.819080175
36790_at	tropomyosin 1 (alpha)	7168	2.209718995	4.39E-10	1.104623941	1.666863013
35766_at	keratin 18	3875	-4.242007604	2.68E-14	-4.656673789	-6.504888937
36791_g_at	tropomyosin 1 (alpha)	7168	2.9249265	8.61E-13	1.468402341	1.880703517
33103_s_at	adducin 3 (gamma)	120	3.920756358	2.92E-10	6.031570788	3.575830825
37785_at	RHO6 GTP-binding protein (?actin cytoskeleton regulation)	27289	4.221025029	2.48E-12	1.273849496	7.406673709
39070_at	fascin (actin-bundling protein)	6624	-2.330745344	6.37E-13	-1.68300774	-2.694414931
35803_at	ras homolog gene family, member E (disassembly of actin stress fibres)	390	-2.233636127	2.29E-10	-1.055779002	1.038111944
34886_at	radixin	5962	2.420953001	1.22E-07	1.584145112	1.542677121
34887_at	radixin (crosslinks actin and integral membrane proteins)	5962	2.278449836	6.64E-08	1.199811512	1.794183039
32847_at	myosin light chain kinase	4638	4.896958824	9.13E-09	18.11380806	2.725943964
40069_at	supervillin	6840	2.682759032	0.0000725	3.169652491	2.028055227
1058_at	WASP 3 (actin-cytoskeleton associated)	10810	-2.097291681	1.68E-07	-1.631969908	-3.144102457
38022_s_at	plectin 1, intermediate filament binding protein 500kDa	5339	-2.557004064	0.0000137	-4.301607614	-3.040635806
40899_at	keratin 19	3880	-6.322934628	1.59E-09	-13.66744481	-8.25383859
41294_at	keratin 7	3855	-4.318997454	0.0000126	-7.499352182	-6.560418569
Complement						
37388_at	tissue factor pathway inhibitor 2	7980	23.78384351	2.22E-13	5.35937334	33.8370157
35664_at	multimerin	22915	-3.742143256	1.5E-14	-9.087085855	-4.496252381
36345_g_at	coagulation factor II (thrombin) receptor-like 1	2150	2.846565472	7.74E-08	4.471805084	4.865728749
39409_at	complement component 1	715	5.781697808	0.00000211	13.33715147	6.459955952
36344_at	coagulation factor II (thrombin) receptor-like 1	2150	5.790500377	1.15E-12	6.773344893	4.683025515
37185_at	PAI-2	5055	3.441427028	0.00000796	3.324772251	1.431092156
33803_at	thrombomodulin	---	-4.010890247	6.01E-11	-4.187934083	-2.823656854
35822_at	B-factor, properdin	629	3.628127319	5.92E-07	19.71747326	3.665782889
40496_at	complement component 1, s subcomponent	716	5.442703249	0.00000145	27.82653223	13.55862174
31825_at	serine (or cysteine) proteinase inhibitor, clade D member 1	3053	3.710911406	1.09E-07	2.145669759	1.468699812
36543_at	coagulation factor III (thromboplastin, tissue factor)	2152	9.446520842	0.0000041	8.829602345	9.990355775
33295_at	DARC	2532	3.201933176	0.00000869	4.74993939	2.160165669

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
Extracellular matrix						
39333_at	collagen, type IV, alpha 1	---	3.294038599	1.4E-10	2.248373685	2.640671802
32551_at	EGF-containing fibulin-like extracellular matrix protein 1	2202	-2.645292659	6.16E-10	-3.672557726	-4.730137915
36929_at	laminin, beta 3 (125kD))	3914	4.113164884	3.73E-12	8.332528001	5.436782952
36659_at	collagen, type IV, alpha 2	1284	2.336145488	4.11E-10	2.675850693	2.28281283
35366_at	nidogen (enactin)	4811	-2.021024484	0.00000479	-2.914727592	-3.017493076
35280_at	laminin, gamma 2	3918	10.39471638	0.0000158	3.017362805	15.60150516
37459_at	collagen, type VIII, alpha 1	1295	3.050351654	0.00000175	3.148028315	5.176396595
32818_at	tenascin C (hexabrachion)	3371	44.41053365	0.00000808	4.803724568	5.681119838
35168_f_at	collagen, type XVI, alpha 1	1307	7.746991041	0.00000406	11.09936614	5.956620288
G-Protein and Miscellaneous Receptors						
32114_s_at	G protein-coupled receptor (A2a receptor)	135	7.585528941	0	8.109402646	8.790666973
34288_at	Orphan G protein-coupled receptor	57007	8.088266305	4.55E-15	27.11397321	30.67795921
38247_at	Orphan G protein-coupled receptor	2150	6.820758815	3.54E-10	8.161820702	7.968953316
32115_r_at	G protein-coupled receptor (A2a receptor)	135	3.353944077	1.11E-10	7.275228636	9.470302722
1105_s_at	T cell receptor beta locus	---	-2.885206906	7.15E-12	-1.709061111	-1.489399158
37645_at	CD69 (cell surface glycoprotein)	969	4.1627256	9.18E-08	4.927757479	4.515514511
39310_at	bradykinin receptor B2	624	5.506990833	8.25E-11	21.40768199	26.48656094
40310_at	Toll-like receptor 2	7097	17.04231159	6.34E-08	41.69446428	92.69458196
33764_at	G protein-coupled receptor 51	9568	-4.114163378	7.43E-08	-6.496935914	-5.999971299
40240_at	G protein-coupled receptor, C5B	51704	3.405092443	3.75E-08	2.244472511	3.779946146
41831_at	low density lipoprotein receptor-related protein 5	4041	-2.020184601	0.00000334	-2.92443917	-1.967658837
41831_at	low density lipoprotein receptor-related protein 5	4041	-2.020184601	0.00000334	-2.92443917	-1.967658837
36059_at	low density lipoprotein receptor-related protein 4	4038	2.167124662	0.00049742	1.712017357	1.571062091
33236_at	retinoic acid receptor responder (tazarotene induced) 3	5920	2.254357183	0.000037	2.573139814	1.387068386
33772_at	prostaglandin E receptor 4 (subtype EP4)	5734	-2.821392903	0.00000285	-3.33146064	-5.979710428
706_at	Glucocorticoid Receptor, Beta	---	2.732594537	0.00000824	1.92549503	2.243726671
38222_at	pyrimidinergic receptor P2Y, G-protein coupled, 6	5031	5.12709451	0.00050913	5.150230333	-1.000345091
37534_at	coxsackie virus and adenovirus receptor	1525	-7.953355635	6.94E-07	-10.03852045	-6.352677218
34975_at	killer cell lectin-like receptor subfamily G, member 1	10219	-7.631896619	0.0000201	-3.597564002	-1.580902467
Interferon-inducible genes						
33304_at	interferon stimulated gene (20kD)	3669	6.368043453	6.66E-16	21.37131919	8.654897863
41140_at	interferon gamma receptor 2	3460	3.843792475	3E-15	6.009122949	4.473233377

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
32700_at	guanylate binding protein 2	2634	3.552701285	1.08E-10	4.864506689	2.105432487
464_s_at	interferon-induced protein 35	3430	2.673886964	3.22E-08	9.148025083	3.018968778
39728_at	interferon, gamma-inducible protein 30	10437	5.774728675	3.99E-07	14.1357142	14.8277104
425_at	interferon, alpha-inducible protein 27	3429	2.762082411	3.66E-09	2.627038307	1.886894848
925_at	interferon, gamma-inducible protein 30	10437	7.680903539	1.26E-12	13.2183993	9.629877375
35735_at	guanylate binding protein 1	2633	2.943798001	3.26E-09	6.637940419	4.567149794
626_s_at	interferon-induced protein 35	3430	2.126602914	2.81E-07	9.365638399	2.209101255
38584_at	interferon-induced protein with tetratricopeptide repeats 4	3437	2.968612864	0.00000601	19.75380759	2.995063164
Proteosome system						
41171_at	Proteosome activator subunit 2	5721	2.632747876	2.94E-08	5.101785113	3.339110072
1184_at	proteasome activator subunit 2, beta	5721	3.562723482	1.92E-12	4.791072135	2.802359636
384_at	Proteosome subunit, beta-type, 10	5699	3.877228796	4.1E-14	5.603185012	3.630961741
38287_at	Proteosome subunit, beta-type, 9	5698	4.659894959	4.78E-08	7.535678146	2.324895346
36600_at	proteasome activator subunit 1	5720	2.628955624	7.22E-11	3.416274304	1.918170839
41184_s_at	proteasome subunit, beta type, 8	---	2.245374672	2.58E-08	3.576681689	1.30914074
Heavy metal binding						
31622_f_at	metallothionein 1F (functional)	---	2.113411119	9.82E-13	1.9075731	2.31466058
36564_at	metallothionein 1E (functional) ? pseudogene	127544	2.12687658	2.86E-09	1.738158583	3.383316024
39120_at	metallothionein 1L	4500	2.155505079	0.00010668	1.438072627	1.49279098
39081_at	metallothionein 2A	4502	3.88346697	9.5E-14	1.07990076	4.037912602
TNF ligand and receptor superfamily						
37611_at	TNF receptor superfamily, member 11b (osteoprotegerin)	4982	22.5815417	1.85E-11	6.732948102	23.80716306
32319_at	TNF (ligand) superfamily, member 4	7292	-2.146064062	1.83E-07	-2.349718558	-3.490304298
31540_at	TNF-receptor superfamily, member 9	3604	14.14497071	1.95E-09	31.32294502	8.13544291
34916_s_at	TNF receptor superfamily, member 4	7293	7.281386913	0.00000036	17.13316176	14.8856408
Histocompatibility						
40370_f_at	HLA-G histocompatibility antigen, class I, G	3135	2.224416431	1.84E-09	2.315139184	1.850745369
37383_f_at	HLA-B	3107	2.813651868	1.31E-11	3.293656671	1.69656681
41237_at	HLA-A	3105	2.592434929	1.07E-09	2.056585976	1.66805547

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
37421_f_at	HLA-F	3134	2.42786464	4.91E-10	3.447090363	2.384322116
32321_at	HLA-E	3133	2.208821209	1.1E-08	1.743423717	1.899995194
35017_f_at	HLA-J (pseudogene)	---	2.662234099	5.97E-10	3.747711512	2.904008691
Miscellaneous						
35320_at	NRAMP2 (divalent metal ion transport)	4891	3.804011587	1.44E-12	3.429131292	3.883439443
40215_at	UDP-glucose ceramide glucosyltransferase	7357	4.897679713	0	3.893723735	4.931113889
31697_s_at	ferritin, heavy polypeptide 1	---	2.105668901	0	1.337516978	1.511895019
33943_at	ferritin, heavy polypeptide 1	2495	3.122808312	2.78E-15	2.663086781	2.529725749
38970_s_at	Nef-associated factor 1	10318	7.45565406	0	10.89386893	7.958276569
38971_r_at	Nef-associated factor 1	10318	9.653298205	5.55E-16	14.75346332	3.797994507
32610_at	LIM domain protein (RIL, tumour supressor)	8572	3.406069789	1.89E-14	4.377680625	3.218415014
33331_at	BENE protein (raft-mediated trafficking in ECs)	7851	-7.359188939	5.55E-16	-46.5789075	-18.37518426
39119_s_at	natural killer cell transcript 4	9235	10.49660235	0	4.836079548	3.470433531
36065_at	LIM domain binding 2	9079	-7.075099306	6.45E-12	-11.70672404	-11.6004516
38332_at	purinergic receptor P2X, ligand-gated ion channel, 4	5025	3.527832595	1.79E-12	6.839982825	3.28582656
41446_f_at	RNA helicase-related protein	---	2.049868207	9.01E-09	2.57850892	3.69227503
38631_at	TNF- alpha-induced protein 2	7127	15.5435756	5.02E-13	25.32299307	20.2440913
40236_at	cationic amino acid transporter 2	6542	4.903862742	3.67E-14	3.663619476	5.136877139
41635_at	Wilms' tumour 1-associating protein	9589	5.790617037	3.86E-13	5.777745597	7.816513232
36550_at	RAB5 interacting protein	54453	4.287401682	1.33E-15	2.893396126	4.240726454
33791_at	deleted in lymphocytic leukemia, 1	10301	-2.154987417	4.84E-07	-2.474972561	-3.124750447
39253_s_at	ras-like protein	5898	2.351506735	7.94E-11	2.022311156	3.104448716
39966_at	chondroitin sulfate proteoglycan 5 (neuroglycan C)	10675	2.079781386	0.00034796	1.723347734	2.787442584
35261_at	glia maturation factor, gamma	9535	4.535654994	3.76E-12	3.146314731	1.355411967
40051_at	TRAM-like protein (translocation of secretory proteins)	9697	-2.023145895	1.16E-09	-2.064329419	-2.568060873
41191_at	palladin (predicted immunoglobulin)	23022	2.402476155	3.82E-11	-1.092945296	2.895126951
38169_s_at	cationic amino acid transporter-2A	6542	12.6862715	0	18.10015779	9.03591152
36175_s_at	HIV type I enhancer-binding protein 2	3097	4.702789112	4.64E-12	5.779921347	6.668812125
33731_at	solute carrier family 7 (cationic amino acid transporter), member 7	9056	6.830303999	5.23E-12	2.785124946	3.448986334
38617_at	LIM domain kinase 2	3985	2.398434304	2.8E-11	3.05797248	3.089108758
1876_at	Guanine Nucleotide-Binding Protein Ral, Ras-Oncogene Related	---	2.740128058	4.06E-11	3.184919976	4.783089817
33371_s_at	RAB31, member RAS oncogene family	11031	2.67768839	9.95E-12	2.885116722	3.022230326

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
39959_at	diubiquitin	10537	154.5481774	2.13E-13	83.39051649	60.80792672
38268_at	solute carrier family 1 member 1	6505	-3.494052945	2.36E-08	-2.323709091	-1.880436681
34678_at	myoferlin (Type II mebrane protein)	26509	-2.461785987	8.1E-11	-2.34118743	-4.428257826
37423_at	sodium/potassium/chloride transporter	6558	5.863341383	8.58E-09	10.30897586	3.262676301
41048_at	PMA-induced protein 1	5366	4.124831328	5.88E-11	5.374932281	2.751035089
1877_g_at	Guanine Nucleotide-Binding Protein Ral, Ras-Oncogene Related	---	2.263857729	3.19E-10	1.36624261	2.955732027
37749_at	mesoderm specific transcript (mouse) homolog	4232	-8.563686441	3.39E-12	-3.738761532	-1.890221954
36711_at	MAFF (binds to oxytocin receptor gene)	23764	2.330148548	2.1E-10	3.660794234	3.509266911
35367_at	lectin, galactoside-binding, soluble, 3 (galectin 3)	3958	2.847428796	2.49E-09	2.186535805	1.966123786
37393_at	hairy homolog (Drosophila)	3280	-2.104729557	0.0000105	-3.227167705	-2.968404609
41362_at	macrophage lipid transporter (ATP-binding)	9619	3.698756129	1.87E-08	3.126761474	2.360268513
40434_at	podocalyxin-like protein	5420	2.479801376	2.27E-10	2.872125804	4.127017341
41554_at	chromosome 8 open reading frame 1	734	4.401795539	2E-10	6.312497146	6.214246908
38430_at	fatty acid binding protein 4, adipocyte	2167	11.71004306	1.76E-08	-2.470683976	2.325955927
40427_at	COX17 (cytochrome c oxidase assembly)	10063	2.3179959	6.44E-09	3.564946719	2.403583185
41168_at	Tapasin (antigen processing)	6892	2.919975741	1.33E-09	4.008077657	3.002345356
38268_at	solute carrier family 1 (member 1	6505	-3.494052945	2.36E-08	-2.323709091	-1.880436681
33900_at	follistatin-like 3 (secreted glycoprotein)	10272	2.357044965	5.76E-08	2.168463959	1.891151792
32606_at	brain abundant, membrane attached signal protein 1	10409	2.154773549	1.85E-07	1.676450671	2.705410717
37168_at	similar to lysosome-associated membrane glycoprotein	27074	2.18129371	0.00000117	5.66836506	3.858733053
1798_at	LIV-1 protein, estrogen regulated	25800	3.806942042	2.54E-07	5.605645413	2.523928805
40153_at	ATP-binding cassette, B2	6890	2.658243189	9.77E-10	6.565992214	2.011052241
39327_at	Melanoma associated gene	7837	3.281662101	3.74E-13	1.840301616	2.456998383
38787_at	promyelocytic leukemia	5371	3.246279259	5.42E-09	5.014441081	1.86657737
33235_at	neuron navigator 3	89795	2.126455294	8.42E-07	7.147716124	3.178133882
40391_at	solute carrier family 22 (organic cation transporter), member 4	6583	3.503572137	1.28E-08	5.751930923	2.915071673
39805_at	ATP-binding cassette, B6 (mitochondrial function)	10058	-3.134810592	0.000062	-3.950118144	-7.557051796
38062_at	guanine nucleotide exchange factor for Rap1; M-Ras-regulated GEF	9771	2.385667595	0.00000123	3.284445082	2.129584571
36700_at	Drosophila Kelch like protein	56062	-2.210141615	0.00000889	-2.068838894	-3.814327142
543_g_at	cellular retinoic acid binding protein 1	1381	2.37806162	0.00058519	12.12054759	3.960310682
40171_at	frequently rearranged in advanced T-cell lymphomas 2	23401	-2.042289921	0.00045387	-1.102930154	-3.45484887

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
38152_at	loss of heterozygosity, 11 (tumour suppressor)	4013	2.090463365	5.18E-07	1.10772429	1.474509395
41419_at	CED-6 protein (?Involved in phagocytosis of apoptotic cells)	51454	2.160266818	0.0000141	2.790711625	2.280229173
40177_at	BRCA2	---	3.632767036	0.0000751	4.837141134	2.256454194
36156_at	aquaporin 1 (channel-forming integral protein, 28kDa)	358	-7.543457532	7.36E-08	-24.72084587	-2.81472244
1451_s_at	osteoblast specific factor 2 (fasciclin I-like)	10631	-2.716285201	0.00096058	-3.058214965	-6.172371916
32052_at	hemoglobin, beta	3043	-2.82310622	0.00061531	-1.063359691	-1.063732475
38267_at	solute carrier family 1 member 1	6505	-2.372362221	0.0001239	-1.854384932	-4.202930496
34232_at	natural killer-tumor recognition sequence	4820	2.060240283	0.00081253	3.524334866	2.678630512
33533_at	DnaJ (Hsp40) homolog, subfamily B, member 4	11080	-3.248997846	1.27E-09	-3.405109343	-4.88373502
31803_at	B7-like protein	23308	8.62168092	6.66E-16	7.351063706	7.831573616
39517_at	HTGN29 protein	56951	2.513008231	8.57E-12	3.043956898	3.301473663
32215_i_at	Rho-related BTB domain containing 3	22836	4.025081573	2.65E-11	1.546933689	3.717203105
31974_at	claudin 14	23562	5.268948019	7.62E-10	16.58450042	14.62230502
38234_at	transducin-like enhancer of split 3 (E(sp1) homolog, Drosophila)	7090	3.190483556	1.01E-08	5.862031912	2.662349924
717_at	GS3955 protein	28951	-5.936942813	1.1E-08	-3.058213083	-3.442126415
34759_at	Human hbc647 mRNA sequence	---	-2.062062602	2.12E-07	-1.090273524	-1.859178255
40314_at	synaptogyrin 3	9143	2.59238833	5.12E-07	3.40394603	2.628868732
1562_g_at	dual specificity phosphatase 8	1850	3.469723923	6.19E-07	2.160285876	1.814944895
34075_at	ring finger protein 3	10336	2.474945089	6.84E-07	1.570008537	1.324684407
158_at	DnaJ (Hsp40) homolog, subfamily B, member 4	11080	-3.069096975	9.69E-07	-5.612414258	-4.225643684
35628_at	transmembrane 7 superfamily member 2	7108	-2.262624361	0.00000127	-7.138287918	-7.896982242
39532_at	Ras and Rab interactor 1	9610	-2.446039394	0.00000369	-2.423287325	-4.576385229
32464_at	defensin, beta 4	1673	5.73206473	0.00000396	9.471669184	5.787182569
40398_s_at	mesenchyme homeo box 2 (growth arrest-specific homeo box)	4223	-2.929695911	0.00000406	-3.319848792	-1.032947415
36691_at	cysteine conjugate-beta lyase; cytoplasmic	883	-2.592484271	0.00000419	-4.781646333	-4.268473905
32285_g_at	T-box 1	6899	-3.404797802	0.00000657	-4.474254059	-1.100885777
35281_at	Human laminin gamma2 chain gene	---	7.305157538	0.0000141	1.253227767	3.632687454
36852_at	Putative prostate cancer tumor suppressor	7991	2.0126302	0.000015	1.834058874	1.163775279
35350_at	B cell RAG associated protein	51363	-2.378507434	0.0000163	-2.826314014	-2.971591523
38223_at	vascular Rab-GAP/TBC-containing	11138	-2.237040168	0.0000198	-2.17332853	-6.419950691
1778_g_at	Ras and Rab interactor 1	9610	-2.039906548	0.0000265	-2.354421127	-2.277558206
34748_at	guanine nucleotide exchange factor for Rap1	25780	4.876306368	0.0000375	1.998297818	1.431030207
38177_at	receptor (calcitonin) activity modifying protein 2	10266	-2.669452927	0.0000544	-1.504408342	-1.725233883
36767_at	cytochrome P450, subfamily I (aromatic compound-inducible),	1543	-3.25254729	0.0000617	-2.335422922	-2.35009816

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
	polypeptide 1					
36103_at	LD78 alpha precursor	---	4.751320817	0.0000661	7.445011283	16.10643497
38916_at	chromosome X open reading frame 6	10046	-2.03566901	0.0000766	-2.600257104	-1.605985898
37695_at	likely ortholog of mouse ubiquitin conjugating enzyme 7 interacting protein 4	9781	-2.301917036	0.00012133	-1.323110698	1.160790171
37452_at	uromodulin (uromucoid, Tamm-Horsfall glycoprotein)	7369	-2.459571854	0.00013772	1.432388832	-2.496391159
38298_at	potassium large conductance calcium-activated channel, subfamily M, beta member 1	3779	2.267192754	0.00014094	1.805996602	2.016570577
34265_at	secretory granule, neuroendocrine protein 1 (7B2 protein)	6447	2.136706898	0.00020271	2.37154058	6.59160987
37420_i_at	major histocompatibility complex, class I, F (	---	6.418888272	0.00020626	12.57659136	4.328385052
1024_at	cytochrome P450, subfamily I (aromatic compound-inducible), polypeptide 1	1543	-2.278885393	0.00021089	-4.433899159	-5.141649045
40604_at	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2	8445	-4.160877249	0.00021373	-1.00374691	-1.088223843
37830_at	transmembrane 4 superfamily member tetraspan NET-5	10867	2.717292959	0.0002566	1.697194729	2.682188088
39579_at	claudin 10	9071	-2.657823461	0.00029297	-1.222678519	-2.151570787
39826_f_at	HIF-1 responsive RTP801	54541	2.730193575	0.00029395	2.196725544	-1.095320201
34432_at	SH2 domain protein 2A	9047	3.310710864	0.00030924	7.989570792	23.07377029
37241_at	paraneoplastic antigen MA2	10687	-2.442605109	0.00032556	-1.856943883	-2.613966323
40606_at	ELL-related RNA polymerase II, elongation factor	22936	2.424019485	0.00037794	3.31621885	2.346164265
1561_at	dual specificity phosphatase 8	1850	3.434679205	0.00038896	1.001924133	1.383633356
39300_at	calmodulin-like 3	810	-3.091045664	0.00042474	1.486878275	-1.021019291
36965_at	ankyrin 3, node of Ranvier (ankyrin G)	288	-2.723182368	0.00044183	-1.044035474	-2.023634007
37514_s_at	mannan-binding lectin serine protease 2	10747	2.200703073	0.00058878	2.16677628	1.730660832
40626_at	metaxin 1	4580	-2.054132333	0.00078486	-1.062883007	-1.186917557
32216_r_at	Rho-related BTB domain containing 3	22836	2.64711066	0.00085998	1.556636149	3.676801387
39680_at	statherin	6779	3.677272808	0.00091313	3.76121132	1.183111878
32944_at	roundabout, axon guidance receptor, homolog 1 (Drosophila)	6091	2.375016818	0.00093376	1.799248044	1.615217552

Table 1b. Genes and ESTs of unknown function, regulated by inflammatory mediators

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
34800_at	AL039458:DKFZp434N0910_s1 Homo sapiens cDNA, 3 end	26018	3.40078204	2.85E-13	2.765010993	6.664710547
38393_at	KIAA0247 gene product	9766	2.29784077	1.67E-09	6.02008351	4.413369148
34678_at	AL096713:Homo sapiens mRNA; cDNA DKFZp564E1616	26509	-2.461785987	8.1E-11	-2.34118743	-4.428257826
39602_at	AL050090:Homo sapiens mRNA; cDNA DKFZp586F1018	25924	-4.577280769	0.0000172	-4.30119521	-10.40709155
38717_at	AL050159:Homo sapiens mRNA; cDNA DKFZp586A0522	25840	-4.689298781	1.28E-08	-7.74893638	-11.28080814
40642_at	cDNA DKFZp564H1916 (from clone DKFZp564H1916)	---	-2.496243538	1.49E-09	-3.8269357	-4.459353442
36336_s_at	KIAA0963	22904	2.332740057	5.13E-09	8.689197154	4.182729484
38510_at	AL049435:Homo sapiens mRNA; cDNA DKFZp586B0220	---	5.396432597	9.74E-11	6.475495162	2.715475488
41690_at	AL049471:Homo sapiens mRNA; cDNA DKFZp586N012	---	3.796753878	2.31E-07	3.480379946	4.086635283
37786_at	Homo sapiens clone 24707 mRNA sequence	---	2.683364137	0.0001284	2.585161023	1.833430515
41837_at	hypothetical protein DKFZp761F2014	56967	-2.367358274	0.0000417	-2.170427473	-2.218598517
35959_at	KIAA0844 protein	22891	3.512525058	0.0000819	1.000129624	1.57103734
36250_at	Homo sapiens clone 24488 mRNA sequence	---	2.099339801	0.0000777	2.646927476	-1.069488008
38749_at	hypothetical protein MGC29643	116372	-6.715917049	0.0000192	-5.323536941	-5.128912423
31849_at	KIAA0564 protein	23078	2.224449383	8.58E-07	-1.476396381	-1.27776956
39827_at	hypothetical protein (HIF-1 responsive)	54541	2.094989151	5.69E-09	-1.05607484	1.073522919
35763_at	KIAA0540 protein	23218	-4.219436032	1.45E-10	-2.077617899	-6.313755213
34176_at	hypothetical protein from clone 643	57228	-2.112126935	1.23E-08	-1.597169536	-1.875122258
41229_at	Homo sapiens mRNA; cDNA DKFZp564H1916	---	-2.2358848	9.58E-09	-2.83431221	-3.1640925
36497_at	hypothetical protein BC011859	113146	-3.616464046	2.82E-11	-4.334097766	-8.757335062
32110_at	KIAA0523 protein	23302	-2.745882047	2.07E-08	-2.214350233	-2.866714311
33325_at	Homo sapiens, clone IMAGE:4151609, mRNA, mRNA sequence	---	2.176427217	6.55E-08	3.266179064	2.671921634
36014_at	hypothetical protein DKFZp564D0462	57211	-5.760412704	3.71E-12	-8.607279686	-9.578098002
40855_at	KIAA1053 protein	23034	2.816692342	2.05E-11	2.161737313	2.608672841
37216_at	KIAA0963 protein	22904	6.46210333	3.22E-13	8.253255749	4.410973232
40472_at	PISC domain containing hypothetical protein	254531	-2.478023126	0.00000857	-1.900414388	-7.223997137
41735_at	KIAA0870 protein	22898	2.356691777	0.0000579	3.836683893	1.946020466
32385_at	Homo sapiens mRNA; cDNA DKFZp566F1224	---	-3.217722448	0.00028948	-1.690512627	-1.478976553
41710_at	hypothetical protein LOC54103	54103	6.540656908	0.0002523	6.153505937	6.999868011
35484_at	Unknown (protein for IMAGE:5177668) [Homo sapiens], mRNA sequence	---	-2.144224745	0.00082522	-3.214996363	-1.249999657
39582_at	Homo sapiens mRNA; cDNA DKFZp586D1122	---	2.047922256	0.00075152	4.318196752	2.0788606
34857_at	Hypothetical protein (?cation-transporting ATPase)	79572	4.947142933	7.33E-15	6.560037706	9.528191509
39597_at	KIAA0843 protein	22885	2.251002894	3.31E-09	1.463446202	1.540119179
38972_at	Hypothetical protein (?mucin protein)	115207	-3.47649954	2.91E-13	-7.807767943	-11.3252609

Probe set	Descriptions	LocusLink	HUVEC FC (n=7)	Bayes.p	HCAEC FC (n=1)	MVEC FC (n=1)
33924_at	KIAA1091 protein (function unknown)	23258	2.032421884	3.58E-08	2.704538654	2.417232497
40239_g_at	hypothetical protein MGC35048	124152	2.19014209	0.00000228	1.613513848	3.423127335
34303_at	hypothetical protein FLJ90798	219654	-4.704828617	0.00000675	-2.511409176	-5.24800397
37030_at	expressed in T-cells and eosinophils in atopic dermatitis	23197	2.060834569	9.18E-07	1.188459581	1.046205726
32791_at	MAC30 (hypothetical protein)	27346	-2.011357014	6.47E-07	-2.174949259	-1.604404811
1529_at	hypothetical protein CG003	10129	-2.488539403	2.91E-08	-3.553893245	-4.186928468
37788_at	Homo sapiens clone 23688 mRNA sequence	---	-2.047017635	0.00028466	-3.046721831	-2.16341444
39837_s_at	Homo sapiens PAC clone DJ0751H13 from 7q35-qter	---	-3.168754335	3.43E-07	-6.848331513	-1.485922984
35861_at	cDNA, 3 end /clone=IMAGE-362388	---	2.102166336	0.00032601	6.510939455	6.956139377

Table 2a: Probe sequences for identification of transcripts of Table 1a

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